

# THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—17TH YEAR.

SYDNEY, SATURDAY, APRIL 19, 1930.

No. 16.

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HARVEY.<sup>1</sup>

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THE Post-Graduate Subcommittee has asked me before the films are shown to give some details of the history of the film and a very short *résumé* of Harvey's life.

First, as to the film. The papers in your hands will tell you how they were prepared as the contribution of University College to the Harvey Tercentenary. Of those who prepared them I need say nothing; if Dale and Lewis are nothing but names to you, you must be far behind in your knowledge of contemporary medicine.

As to how the films came here is another matter. Dr. Rowden White, of Melbourne, Physician to Saint Vincent's Hospital, while in London in 1928 saw the films at the Tercentenary and was greatly impressed by them. He was also fired with the desire to make them available to those of his colleagues in Australia who were unable to attend the celebration. He therefore obtained permission from the College of Physicians to secure copies of the films and brought them out with him to Australia and has arranged their showing through the local branches, first at Melbourne, then at Adelaide, then at Sydney and finally here. The value of this public-spirited action you will be better able to appreciate after you have seen the films.

Now, as to Harvey himself. Most of us, I suppose, know that he was a physician, that he lived in the time of Charles I and the Commonwealth and that he discovered the circulation of the blood, possibly also that he did original work on embryology and anatomy and that he was much loved by all who knew him. Well, here is a little more detail.

He was born at Folkestone in 1578 and was educated at Canterbury and Caius College, Cambridge.

At the age of twenty he went abroad to study medicine, especially anatomy, at Padua.

Nowadays our medical schools hold that before the end of his third year, a medical student must have dissected the body twice completely. At Caius College, specially favoured by law, the bodies of two criminals were received annually for dissection. At Padua it was only the favoured few who might actually do any dissection. Most of the anatomy was done by the lecturers, lecturing before their classes. In a class of over a hundred the "back benchers" probably learned very little and the anatomical knowledge of the medical profession as a whole was not high. There is a picture of Vesalius lecturing to such a gathering.

The use of preservatives as a rule was very ineffective, so that dissections had to be done hastily

and naturally the soft parts were often very badly shown and thus it is not surprising how things that today seem obvious, were actually a matter of error for centuries. But, at the same time, there were permanent preparations made of the soft tissues which showed great skill.

Take the valves of the heart for instance. To us their function seems entirely obvious, but although Vesalius figured them most graphically, yet it was only Harvey who explained their function.

Of physiology as we know it, there was nothing at all and experiment, to prove contentions over argument and appeal to authority of the ancients, was only just beginning to appear.

Such was the teaching of the basic sciences of medicine.

The film will show you what was the conception of the circulation of the blood prior to Harvey's work and you will again be inclined to say how they failed to appreciate the obvious. But an old teacher of mine used to say that an inability to appreciate the obvious was the commonest fault in medicine.

How great the weight of tradition was at this time, it is most difficult for us to realize. The mere fact that Galen or Hippocrates had made some pronouncement in medicine or science, settled the matter for all time.

There is a story of a philosopher only a century before Harvey who, in an argument on the teeth of horses, appealed to the horse against Aristotle. He narrowly escaped burning for heresy. The battles of Darwin and Huxley for the doctrine of evolution, the fight which Lister and Pasteur fought for the doctrine of infection, and the bitter religious-scientific feud against Morton and Simpson before anaesthetics were adopted, are today difficult to realize; but they were nothing to Harvey's disturbance of existing ideas and ways of thought.

His modest statement that the ancients were well worthy of study, yet they did not know everything, summed up his whole attitude—an attitude which incidentally was a revival of the real spirit and methods of Galen and Hippocrates, Aristotle and Hipparchus.

Harvey worked at Padua for four years and was especially singled out by Fabricius, the great Professor of Anatomy, and probably carried out some of the dissections used by Fabricius in his work on the valves of the veins. Harvey himself afterwards told Boyle that it was these valves that first attracted his attention to the circulation of the blood.

In 1602 he was admitted Doctor of Medicine at Padua. Harvey's sojourn at Padua was exactly the counterpart of the stay of the modern overseas practitioner who spends a period in London or Vienna and takes out a higher degree therein.

In England he took his M.D. at Cambridge and his M.R.C.P. in 1604 and his F.R.C.P. in 1607 and in 1609 he became Physician to Saint Bartholomew's Hospital.

<sup>1</sup> Read at a meeting of the Queensland Branch of the British Medical Association on February 7, 1930.

In 1615 he was elected Lumleian Lecturer in which office his lectures were on anatomical subjects, and in his manuscript notes of his first lecture in 1616 is the first actual statement of the circulation of the blood.

One remarkable fact is that owing to lack of a microscope Harvey never demonstrated the capillaries; he only deduced the necessity for their existence, an existence actually demonstrated by Malpighi, six years after Harvey's death.

It was not until 1628, however, that he actually published his epoch-making book, one of the few books indeed to which this epithet can be applied.

He had almost at once acquired a notable practice, had as one patient Francis Bacon (who expounded in his "*Novum Organum*" the principles which Harvey so diligently applied) and was appointed Physician Extraordinary to James I, later, in 1631, Physician in Ordinary to Charles I. The latter was interested in his physician's anatomical zeal and gave him a liberal supply of the bodies of deer, then a Royal prerogative, for dissecting purposes.

He followed the King's fortunes in the Civil War and at the Battle of Edgehill in 1642 he was placed in charge of the King's children.

At Oxford, the Royalist headquarters, he remained until it surrendered in 1646 and then returned to London, living privately with his brothers. In 1651 was published his great work, the "*De Generatione Animalium*."

In 1657, after some years of martyrdom from gout, he died of cerebral hæmorrhage.

Accurately to appreciate Harvey's greatness, it is essential to compare him with his contemporaries.

In England, at this time, there were two classes of practitioners, the regular physicians, usually graduates of Cambridge or Oxford, later admitted Members and Fellows of the College of Physicians, while outside there was an enormous variety of irregular practitioners, of whom the physician astrologers were the most important.

An example of these is Dr. Nicholas Culpeper, who wrote various books, including a herbal, which was being reprinted in 1862 and which was apparently a standard work for two hundred years. Of his style, let me give you two extracts, the one an opinion of his enemies, the College of Physicians, and the other the use of foxglove or digitalis which only a few decades later was to be used in an entirely modern way by Withering.

Of foxglove he writes:

The purple Foxglove is an herb of Venus, and so is Mightily useful in those female disorders which are born of love, notably the "green sickness," the decline and the greater hysteria. A confection of the leaves well pounded with vinegar may be put to the temples in the Green-sickness, and an infusion drunk hot at bed time will calm the blood and humours in disappointed love. The flowers, soaked in wine, may be taken thrice daily in the melancholic states of hysteria, while a cordial made from the flowers, essence of ginger, tincture of cardamons and aqua vitæ is a mighty keeper up of the heart in times of plague and pestilence.

His opinion of his more orthodox colleagues was bitter enough:

Drones that do but steal the honey and contribute not one drop in exchange, like to the Fellows of the College of Physicians.

These do but sit in London and with much crying up of their learning, because forsooth they have been at Oxford or Cambridge, and who yet without having seen a sick man, or knowledge of the Planets, will pretend to treat all diseases with a skill and knowledge above others who have laboured a lifetime therein. So are poor simple folk misguided and the rogues flourish.

At least Dr. Culpeper's pharmacy did not include the loathsome and useless animal preparations which were included in the London Pharmacopœia of 1627, such as powdered mummy to resist gangrene, human skin probably as a ligature, powdered shark's tooth for scorpion bites, ends of scorpion tails as a diuretic, callosities of the knees of horses for epilepsy, human blood as a sudorific and diaphoretic, human vesical calculi for stomach troubles and powdered human skull for epilepsy.

But of Dr. Culpeper the best possible picture is given by Mr. Kipling in his story, "A Doctor of Medicine," and the whole spirit of his medical knowledge is summed up in the lines:

Wonderful little when all is said,  
Wonderful little our fathers knew,  
Half of their remedies cured you dead—  
Most of their teaching was quite untrue.

Look at the stars when a patient is ill  
(Dirt has nothing to do with disease).  
Bleed and blister as much as you will,  
Blister and bleed him as oft as you please!

It is probable that many of the regular physicians were little better, but, above all, they had Harvey setting a new standard—he experimented. It is as a medical experimentalist and as a shatterer of preconceived ideas that Harvey shone and it is just these qualities which are most needed in medicine today.

Of his use of the experimental method the film will tell you, as a shatterer of authority stands his attitude of a profound scepticism of anything which ran counter to his own experience.

Not only in physiology but in practical medicine was Harvey an innovator and that in a branch which is today receiving greatly increased attention—midwifery.

When Harvey began to practise, the art of obstetrics was neglected and there was no original work in midwifery in the English language. The ordinary practice of midwifery was in the hands of midwives, very ignorant and very prejudiced. They were bitterly opposed to the doctors who were called in only to difficult and operative cases which were often rendered fatal by the ignorance and brutality of the midwives.

Harvey, however, attacked embryology, gynaecology and midwifery, so that his book "*De Generatione Animalium*" is at once a record of scientific research and a practical text book.

With at most a hand lens he studied the developing chick and his only errors were those due to his lack of a compound microscope. Note his fundamental generalization: "*Omne vivum ex ovo*."

This book was published in 1651 and one chapter, "*De Partu*," is the first English work on midwifery with evidence of much practical experience in the art. Very modern, even allowing for the greater hazard of interference in those long preantiseptic days, is his recommendation of patient watching and gentleness in ordinary cases.

He had seen and recognized adherent placenta, ectopic gestation, survival of an infant delivered by Caesarean section several hours after the death of the mother, the mechanism of breech presentation, involution of the uterus and almost all the essential features of modern obstetrics; in gynaecology he knew displacements, spurious pregnancy, various forms of cancer and internal hæmorrhages.

His friend Willoughby, no mean obstetrician himself, wrote of Harvey as "that most worthy good and learned Doctor, whose memory ought to be held for ever in great esteem with midwives and child bearing women."

Naturally, Harvey's work did not find immediate acceptance. There was much bitter opposition, but it finally found general acceptance in his lifetime. Unlike such discoverers as Mayow, who studied oxygen a hundred years before Lavoisier, Mendel who was the pioneer in heredity, Boddington, of Sutton Coldfield, whose advocacy of open air treatment was half a century ahead of its time, he lived to see it accepted and himself acclaimed.

It may be asked: "What good does this history of medicine do?" "Why should we recall these early workers and their often incomplete work?" "Of what benefit can Harvey's crude preparations and experiments be to our present generation?"

I think the answer is first that none of us is so brilliant that he cannot learn from the past. We may not find a use for Harvey's experiments in our daily practice, but Harvey's attitude, especially his willingness to learn from clinical material and from experiment, is one which we should all faithfully copy.

There is too, running all through medical history, with examples so few as to be all the more glaring, a strain of devotion to work and duty which our profession can never afford to let go.

Let Mr. Kipling again speak of Dr. Culpeper and his time.

Yet when the sickness was sore in the land,  
And neither planet nor herb assuaged,  
They took their lives in their lancet-hand  
And, oh, what a wonderful war they waged!  
Yes, when the crosses were chalked on the door—  
Yes, when the terrible dead-cart rolled,  
Excellent courage our fathers bore—  
Excellent heart had our fathers of old.  
None too learned, but nobly bold,  
Into the fight went our fathers of old.

#### Acknowledgements.

In preparing this paper I consulted the following authorities: "The Evolution of Modern Medicine," Osler; Garrison's "History of Medicine," "Harveian Orations," 1920-1927; Introduction to Everyman's Library Edition of "*De Motu Cordis*," by E. A. Parkyn; "The British Herbal," 1862, by Nicholas Culpeper.

#### EXPERIMENTAL ANÆSTHESIA WITH TRI-BROM-ETHYL-ALCOHOL ("AVERTIN") AND SODIUM ISO-AMYL-ETHYL-BARBITURATE ("SODIUM AMYTAL").

By ADOLPH BOLLIGER, Ph.D.,

AND

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DURING the course of an investigation of nephritis in dogs and puppies, we became dissatisfied with inhalation anæsthesia under which the frequency of bronchopneumonia considerably restricted our material, aided, probably, by the preliminary resection of the vocal cords necessary to quieten dogs when quartered near hospital wards. The first and natural alternative which suggested itself was induction of anæsthesia by the rectal route. A trial was made of Gwathmey's oil-ether technique in the dosage recommended by him for dogs,<sup>(1)</sup> but this seems a complicated procedure besides requiring beforehand a large depressant dose of morphine. "Avertin" (tri-brom-ethyl alcohol) became available locally about this time and led us to make trials of experimental anæsthesia with this new drug.

Before this work was concluded, we were also furnished with a supply of "Sodium amytal" (sodium iso-amyl-ethyl-barbiturate), a white powder soluble in distilled water which has been used in the United States of America as an intravenous narcotic. We therefore decided to test the suitability or otherwise of this substance for our work and to criticize it according to the standards we had already applied to "Avertin."

#### "AVERTIN."

Considerable animal experimentation has already been done with "Avertin" in an attempt to establish its pharmacological reaction and clinical usefulness. A certain portion of this work seems to be still contradictory and an opportunity presented itself of repeating a part dealing with one or two of these questions.

Furthermore, apart from assessing the value of "Avertin" as an experimental anæsthetic, we were particularly desirous of testing it according to certain metabolic criteria and effecting a comparison thereby with certain inhalation anæsthetics in the manner already shown.<sup>(2)</sup>

Also operative work planned on animals with advanced X ray nephritis led us to investigate the alleged contraindication of nephritis toward "Avertin" anæsthesia.

With these purposes in mind we studied the following blood constituents during and after "Avertin" anæsthesia: (i) Changes in the acid-base equilibrium of the blood as measured by the carbon dioxide combining power of the plasma, (ii) blood sugar, (iii) inorganic phosphates of the blood plasma, (iv) cholesterol content of the blood.

Observations were also made upon the urinary output with regard to volume and phosphorus content.

The experimental material included: (i) Normal dogs and puppies, (ii) normal dogs undergoing major operative interference, (iii) dogs with experimental nephritis of varying degree.

#### Methods.

##### Administration.

The "Avertin" solution is first prepared according to the standard instructions, 0.4 to 0.5 gramme of "Avertin" liquid per kilogram body weight of dog being used. These instructions are set out in "Avertin, the Basal Narcotic," a booklet published by Bayer Products, Limited, London, 1929. Solution of the drug is considerably hastened by rapid shaking in an Erlenmeyer flask and raising the temperature up to 50° C. We failed to observe any ill effect or decomposition as a result of heating to this figure.

The dog is held by his hind legs and tail with head downwards. A lubricated rubber catheter is passed well up the bowel, ten to twenty-five centimetres (four to ten inches). The warm solution is slowly injected by means of a syringe or gravity, the catheter withdrawn and the anus kept well closed by firmly clamping together the long hairs on opposite sides of the anus, the object from first to last being to preserve if possible every cubic centimetre of the injection. Unless this necessity is appreciated and all the above precautions taken, early relaxation of the *sphincter ani* will cause a loss of a large amount of the anæsthetic. Curved rubber-covered intestinal clamps can be used to close the anal orifice without causing the dog any apparent pain. It is usually recommended to wash out the bowel first, before administering the solution, but we have found after using it frequently that no advantage followed. Merely holding a wool tampon over the anus is not enough to prevent regurgitation.

##### Biochemical Methods.

The following biochemical methods were used:

1. The carbon dioxide combining power of the plasma was determined by the method of Van Slyke and Cullen.<sup>(3)</sup>
2. The blood sugar was determined according to the method of Hagedorn and Jensen.<sup>(4)</sup>
3. The inorganic phosphates of blood plasma have been determined by the method of Benedict and Theis.<sup>(5)</sup>
4. The cholesterol content of the plasma was estimated according to Grigaut's method as modified by Day and Bolliger.<sup>(6)</sup>

##### Experimental Details.

##### "Avertin" Anæsthesia in Normal Dogs Without any Operative Interference.

There were thirty dogs in this series. A typical example of the blood changes in this group is seen in Chart I. This chart represents the changes found in a healthy dog of seventeen kilograms body weight.

After a night's fasting eight cubic centimetres of "Avertin" liquid representing 0.47 gramme per kilogram were administered following a preliminary colonic lavage. The induction was rapid and satisfactory, the animal exhibiting no signs of discomfort or fear, until it suddenly fell asleep two minutes after the injection was complete. Complete anæsthesia with perfect relaxation ensued, lasting one hour. Pulse rate was slightly quickened (by about ten beats per minute). Respiration became deeper and slower, while the mucous membranes remained quite pink. After an hour's narcosis, during catheterization the animal yawned, corneal reflex and muscular tone returned and it began to stagger about within another half hour. Two hours later the animal was still somewhat ataxic, but eating. By three hours the animal had fully recovered. Reference to Chart I shows the following variations in carbon dioxide combining power of the plasma, blood sugar and blood phosphates.

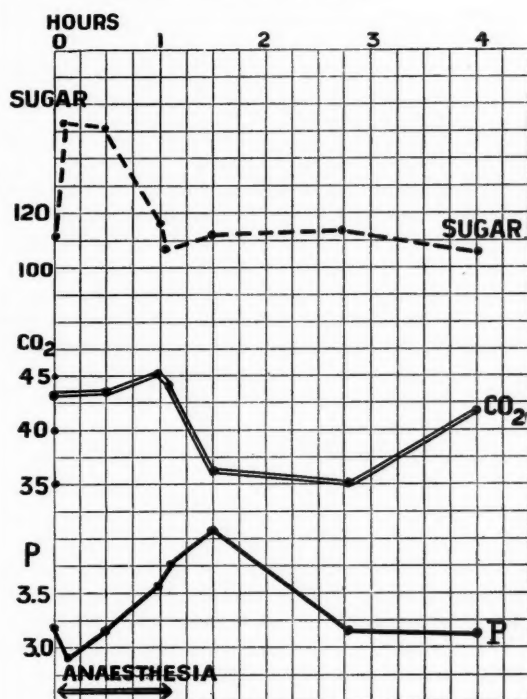


CHART I.

"Avertin" anæsthesia in a normal dog. P = inorganic phosphate of the plasma in milligrammes per centum. CO<sub>2</sub> = carbon dioxide combining power of the plasma in volumes per centum. Sugar = blood sugar in milligrammes per centum.

**The Carbon Dioxide Combining Power of Plasma.** The carbon dioxide combining power of the plasma remained almost completely normal throughout the whole period of anæsthesia, as shown by consecutive determinations during the first hour. Half an hour after recovery a slight but distinct drop was noted and persisted thus for a further hour and a half. Three hours later the carbon dioxide combin-

ing power was found to be at the preexperimental level.

**Inorganic Phosphates.** A slight fall in the inorganic phosphates was apparent immediately after injection, followed in half an hour by a rise to the preexperimental level. From this the phosphates rose steadily for ninety minutes to a point about one milligramme higher than the preexperimental level. Thereafter a fall set in, the original figure being reached and maintained by two hours after recovery from anaesthesia.

**Blood Sugar.** As with the inhalation anaesthetics, the blood sugar rose immediately after induction, showing an excess of thirty milligrammes per hundred cubic centimetres over normal which was maintained for half an hour. Thence it fell to a corresponding degree at the end of the period of narcosis (one hour) and after this it remained within normal limits for dogs.

The further subjects of the same series with one exception demonstrated similar variations in blood chemistry. Another was purposely given a distinct overdose of anaesthetic equivalent to about 0.65 gramme per kilogram. Anaesthesia, lasting one hundred minutes, ensued. The behaviour of the inorganic phosphates, though varying more sharply in degree, was essentially the same as before, the preexperimental level being reached at four hours. As regards the carbon dioxide combining power, the postanæsthetic fall was not remarked during the time limits of the experiment. The maximum rise shown by the blood sugar and observed twenty minutes after induction was only ten milligrammes per hundred cubic centimetres. Another animal which received an overdose amounting to 0.6 gramme per kilogram, died a few minutes after induction.

Further, we have seen death occur from respiratory failure forty minutes after induction with a carefully measured dose of 0.5 gramme per kilogram. This dosage, nevertheless, is considered within normal limits and in many other instances was found to produce satisfactory anaesthesia. The animal, although having fasted for twenty-four hours, was normal in every respect and this death was entirely unforeseen. Observations on the blood in this instance are interesting, as they showed a progressive rise of inorganic phosphates from 3.9 milligrammes to 5.5 milligrammes at death. The blood sugar rose from 70 milligrammes to 141 milligrammes at death.

#### Normal Dogs Undergoing Major Operative Interference.

The series of normal dogs undergoing major operative interference, about fifty in number, includes dogs on which such severe surgical procedures as laminectomy, transplantation of ureters, nephrectomy *et cetera* were carried out. Chart II illustrates the blood findings under "Avertin" in a dog of eighteen kilograms body weight, while portions of the posterior nerve roots of the spinal cord were excised for the purpose of another inves-

tigation. In spite of the extensive character of the operation, involving considerable blood loss and primary shock, perfect anaesthesia was obtained for the whole period of the operation (fifty minutes). With regard to carbon dioxide combining power of plasma and blood phosphates, the changes were of the same order as in Chart I.

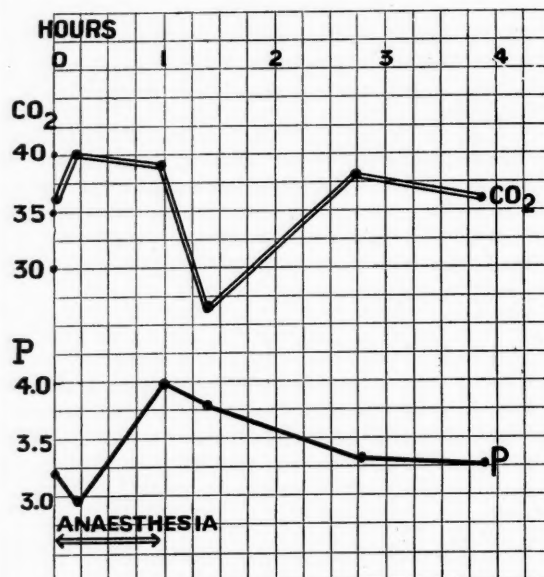


CHART II.

"Avertin" anaesthesia in a normal dog undergoing severe major operation. P = inorganic phosphate of the plasma in milligrammes per centum. CO<sub>2</sub> = carbon dioxide combining power of the plasma in volumes per centum.

#### "Avertin" Anaesthesia in Dogs Suffering from Experimental Nephritis.

"Avertin" anaesthesia was used in dogs suffering from various degrees of unilateral chronic interstitial nephritis induced by direct irradiation of the kidney, with subsequent removal of the healthy kidney. Further details of this procedure were given in communications concerning the same animals, which appeared recently.<sup>(7) (8)</sup>

Biochemical observations were made first on dogs suffering from moderate nephritis and during a mild anaesthesia, for example, dogs with a blood urea before anaesthesia of 108 milligrammes per 100 cubic centimetres (*vide* Chart III). This dog was given 0.4 gramme per kilogram; anaesthesia lasted twenty-five minutes and relaxation was incomplete. The blood phosphates in this degree of nephritis are still within normal limits. Fourteen minutes after induction there was a slight fall, normal figures being regained after half an hour. Carbon dioxide combining power before the experiment showed a level of 30% (minimum normal limit equals 34%).

This figure (30%) was maintained during the anaesthesia, but afterwards showed a slight rise of 5%. Blood sugar remained fairly steady through-

out. Figures for blood urea failed to rise and no elevation could be found on the following day.

Another dog was selected suffering from a more severe degree of nephritis. In this animal blood urea was 256 and carbon dioxide combining power 25%. Light anaesthesia was induced, lasting ten minutes, by the administration of 0.38 gramme per kilogram. Carbon dioxide combining power rose slightly during and after narcosis and phosphates rose from four to five milligrammes. None of these dogs appeared to feel any ill effects from the above experiments, so we considered that a more crucial

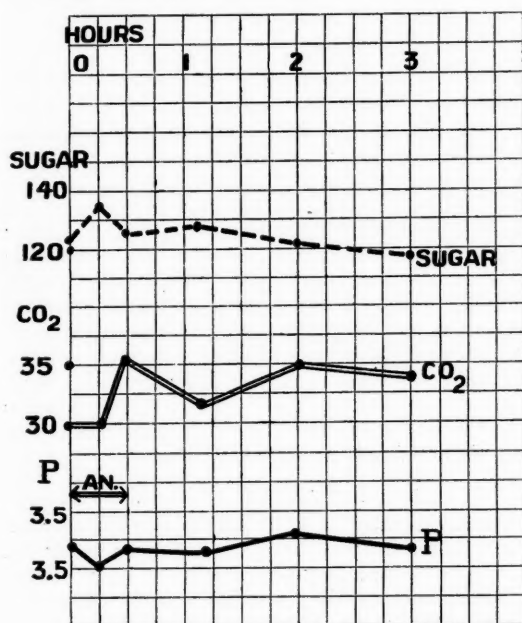


CHART III.

Short "Avertin" anaesthesia in a moderately nephritic dog. (Blood urea 80 milligrammes per centum.) P = inorganic phosphate of the plasma in milligrammes per centum. CO<sub>2</sub> = carbon dioxide combining power of the plasma in volumes per centum. Sugar = blood sugar in milligrammes per centum.

trial would be to select an animal with still further advanced nephritis. The dog chosen was considered a bad "risk," being drowsy, somewhat oedematous, with a rapid pulse and from previous experience was allowed a maximum vital expectancy of about two weeks. Zero blood readings were as follows in milligrammes per hundred cubic centimetres: Blood urea, 248; phosphates, 5.1; carbon dioxide combining power, 13%; cholesterol, 222.

A dose of 0.45 gramme of "Avertin" per kilogram body weight was administered and the animal remained unconscious for ninety minutes, showing all the features of a deep anaesthesia with at times very slow respirations. This period of narcosis was in excess of what would be expected in a normal dog, and the animal showed unusual delay during recovery in acquiring full muscular control, staggering about for two hours in a drowsy state. It then

ate some meat. Next day it was apparently quite unaffected by the experience or if anything more alert than previously and it had a blood urea of 195. Chart IV illustrates the biochemical variations.

1. Inorganic phosphates rose from the original level of 5.1 to 6.6 milligrammes one hour after induction. At recovery point they were 7.1 milligrammes. One and a half hours later they reached 6.2 milligrammes, in another hour 5.6 milligrammes. This indicates a considerably slower return to normal than usual.

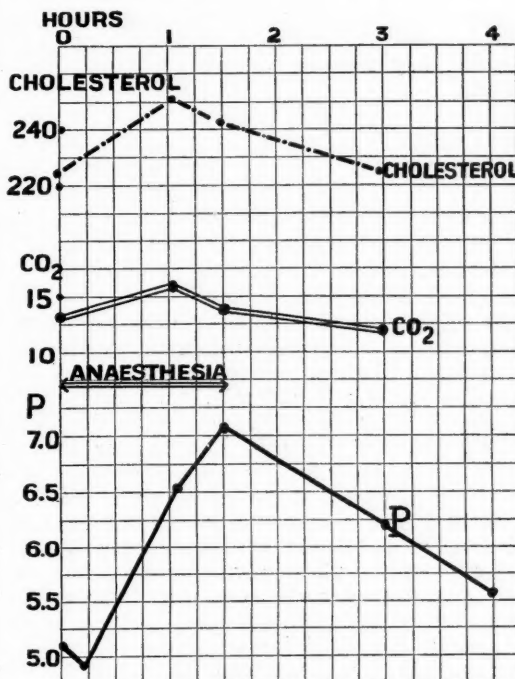


CHART IV.

Prolonged "Avertin" anaesthesia in a severely nephritic dog. (Blood urea: 248 milligrammes per centum.) P = inorganic phosphate of the plasma in milligrammes per centum. CO<sub>2</sub> = carbon dioxide combining power of the plasma in volumes per centum. Sugar = blood sugar in milligrammes per centum. Cholesterol = cholesterol of the plasma in milligrammes per centum.

2. Carbon dioxide combining power did not alter appreciably during narcosis, but one and a half hours after recovery there was a slight fall. Next day the carbon dioxide combining power was 16%, that is, somewhat higher than the extremely low preexperimental level.

3. Blood cholesterol rose slightly during anaesthesia, in accordance with the findings of Mahler,<sup>(9)</sup> without any further postanesthetic change.

#### *The Effect of Repeated "Avertin" Anaesthesia on the Normal Liver.*

One further experiment was performed on a healthy young dog to detect any possible harmful effect of the drug on the liver following frequently repeated "Avertin" anaesthesia of moderate dura-

tion. The dog selected was fully within normal standards. Within twenty-four hours it received five potent injections of "Avertin" of increasing strength, ranging from 0.5 to 1.0 gramme per kilogram.

The total period in which the animal was completely under the influence of the drug was five hours. After finally regaining consciousness, the animal appeared none the worse for its experience, as judged by clinical standards. It exhibited no trace whatever of jaundice. On the following day the animal, still in apparent good health, was killed and submitted to autopsy. Macroscopical and microscopical examination of the liver and kidneys failed to reveal any increase of fat or other sign of toxæmia.

#### "SODIUM AMYTAL."

We employed "Sodium amytal" under exactly the same conditions as "Avertin." Similar, and in some cases the same, normal and nephritic dogs were used, so that we were enabled to make a fair comparison between it, "Avertin," and other inhalation anaesthetics.

#### Method of Administration.

The original pharmacological work in amytal anaesthesia was first performed in the laboratories of Eli Lilly, Limited. Subsequently it was first applied to man and extensively studied at the Indianapolis City Hospital. Following the advice of these workers<sup>(10)</sup> we commenced our inquiry, using a dose of forty to fifty milligrammes per kilogram body weight of the dog. This was dissolved in distilled water and slowly injected into the saphenous vein. Rapid anaesthesia ensued, sometimes even before injection was complete. In some cases a transitory excitement stage was evident which may be sufficiently pronounced to interfere temporarily with the injection process. The above workers state that anaesthesia is not sufficiently deep for surgical procedures before twenty minutes have elapsed, but in our experience it is not necessary to wait for more than half this period. Relaxation has been sufficiently complete, respirations slow and the pulse hardly altered. When the above dose was used, the average duration of complete anaesthesia varied from one to three hours. Long operations involving interference with richly innervated structures may require a small addition of ether by inhalation if a fairly large dose has not been given. The recovery period is particularly long, lasting from two to sixteen hours, depending on the dose used.

The first sign of recovery from deep anaesthesia is a manifestation of a "stretching" reflex elicited by hyperextending a hind limb, whereupon the animal slowly extends its back and all four limbs. This sign is of value, as it appears very early in the recovery phase when relaxation is complete and the corneal reflex absent. During recovery also, a return of the excitement phase is frequent, the animal making continuous movements of locomotion with the fore limbs. Even after standing

upright the animal remains ataxic with pronounced weakness of the hind limbs, though quite interested in its surroundings. We found we usually could produce an anaesthesia with a dose of thirty-five to forty-five milligrammes per kilogram which was quite enough for operations such as nephrectomy.

#### Experimental Results.

About a hundred dogs and twenty puppies were anaesthetized in this manner with very satisfactory results and no deaths. This material could be roughly divided into the same groups and the same biochemical procedures were followed as in the case of "Avertin."

#### Normal Dogs.

We were able to confirm in all respects the same findings in regard to dogs as the American observers have found in regard to dog and man, namely, a clinically satisfactory and non-toxic anaesthesia. With respect to the biochemical findings, the blood sugar level displayed a very slight rise some time after induction, but not immediately as with other anaesthetics and of a slighter degree than ever observed previously. The carbon dioxide combining power of the plasma remained constant both during and after the period of full anaesthesia. As noted with "Avertin," the blood phosphate sometimes showed a slight fall just after narcosis began. In a long anaesthesia there was a slight increase above the preexperimental level during the period of maximum depth of narcosis.

#### Dogs with Renal Insufficiency.

We concentrated our attention particularly on dogs with renal insufficiency in order to study the influence of renal insufficiency on sodium amytal anaesthesia and as they provide a better means of assessing the value of the drug in the sick or potentially sick organism in which metabolism as a whole and especially the acid base balance is already deranged. As before, these dogs were suffering from renal insufficiency of all grades, induced by direct irradiation of one kidney followed by removal of the other or by bilateral implantation of the ureters into the intestine.

An example of the changes observed during prolonged anaesthesia (over five hours) in a slightly nephritic dog with a blood urea of fifty milligrammes per hundred cubic centimetres is seen in Chart V. This dog weighed fifteen kilograms and received a dose of forty-eight milligrammes per kilogram body weight. In this dog deep narcosis was so prolonged that after five and a half hours forty milligrammes of ephedrine sulphate were injected. Soon afterwards the animal showed signs of recovery and after eight hours had thoroughly recovered. In spite of this deep and lengthy anaesthesia the biochemical findings were practically normal as regards carbon dioxide combining power, blood sugar and cholesterol. The blood phosphates showed a slight elevation during the second and third hour of anaesthesia.

Animals with more severe renal insufficiency were found to require distinctly less sodium amytal to produce full anaesthesia. Two similar dogs which had an insufficiency of long standing, had a blood urea level in the neighbourhood of one hundred milligrammes per hundred cubic centimetres in both cases. A dose of thirty-six milligrammes of "Sodium amytal" was sufficient to produce anaesthesia lasting one hour in one dog and nearly two hours in the other. The period of recovery in one was marked by excitement and in the other was smooth.

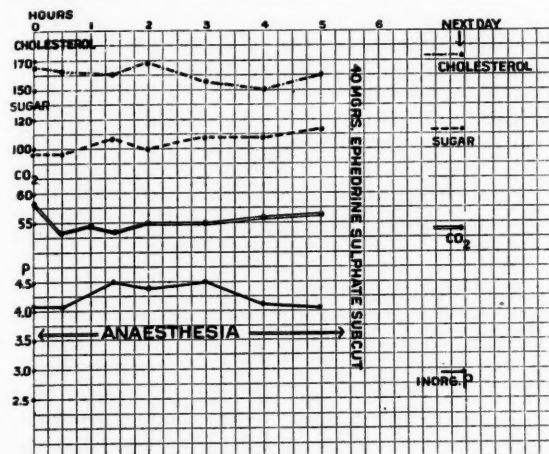


CHART V.

Prolonged "Sodium amytal" anaesthesia in a slightly nephritic dog. (Blood urea 50 milligrammes per centum.) P = inorganic phosphate of the plasma in milligrammes per centum. CO<sub>2</sub> = carbon dioxide combining power of the plasma in volumes per centum. Sugar = blood sugar in milligrammes per centum.

In a further experiment it took only twenty-seven milligrammes to produce an anaesthesia lasting for one half-hour. In this instance the renal insufficiency was due to implantation of the ureter into the intestine. This dog showed a blood urea of 135 milligrammes and a carbon dioxide combining power of the plasma of 30% at the time of the experiment. Such a small dose in a normal dog would be expected to produce only excitement. Even more conclusive was the case of another dog with a similar type of renal insufficiency where full and satisfactory narcosis of forty minutes' duration followed the administration of only twenty milligrammes of "Sodium amytal" per kilogram of body weight. Though this particular dog had a blood urea content of 240 milligrammes, there were no clinical signs of a toxæmia.

In a uræmic, weak and emaciated animal (blood urea 340 milligrammes) it took only fourteen milligrammes per kilogram of body weight to produce an anaesthesia with complete relaxation of thirty minutes' duration. At this stage of our study our limited supplies of "Sodium amytal" became exhausted. As a result we were unable to test to our satisfaction other aspects of this type of anaesthesia, for example, the experimental value of the so-called antidote.

## DISCUSSION.

The advent of such potentially dangerous anaesthetic agents as "Avertin" and "Sodium amytal" into general clinical use demands a most thorough and exhaustive inquiry into their pharmacology which should be reviewed in the light of every available standard.

The general objection to such anaesthetics as "Avertin" and "Sodium amytal" where anaesthesia, once induced, does not permit of regulation as in the case of the inhalation anaesthetics, is well recognized and also appreciated by us. This aspect of the subject naturally is less significant in the laboratory animal than in the human patient.

## "Avertin."

The clinical contributions on the subject of "Avertin" are numerous, while the biochemical reactions of the blood and urine have received but scant attention. Extensive but purely pharmacological work has been done by Straub,<sup>(11)</sup> Eichholtz,<sup>(12)</sup> Lendle,<sup>(13)</sup> Bender<sup>(14)</sup> and others, and more recently in England by Parsons.<sup>(15)</sup> This brief study, therefore, arising as a side issue from other experimental work, confines itself mainly to the consideration of a few points on the question of the biochemical response of the organism to "Avertin" anaesthesia, to the compatibility or otherwise of nephritis with this form of narcosis and to a criticism of such anaesthesia when used for experimental purposes.

To the laboratory worker the disadvantages of the inhalation anaesthetics in animal experimentation need no emphasis and "Avertin," besides minimizing the risk of respiratory complications, frees an assistant to aid the operator, once the narcosis is complete. With a dosage of 0.4 to 0.48 gramme per kilogram of body weight the anaesthesia has usually been of satisfactory depth and duration for smaller operations, but frequently a small amount of ether has been necessary in larger operations. The close observations required in physiological and biochemical work are not distorted by fear or struggling and the animal sinks gently to sleep. About thirty puppies of all ages received the drug for the purpose of exposing the kidney. Here the question of accurate and careful dosage becomes of great importance, often puppies of the same litter and degree of development seeming to differ in the degree of tolerance to the drug. We have concluded that in general a dose of 0.4 gramme per kilogram of body weight is the average optimum for dogs, supplemented, if necessary, and after waiting for fully ten minutes, by a very small quantity of ether by inhalation. A sudden high concentration of inhaled ether vapour after "Avertin" is very prone to cause a sudden respiratory spasm with reflex arrest of the heart, from which recovery was not observed. We have not found preliminary washing out of the bowel of any particular advantage, as only a small quantity of distilled water is required as a vehicle, providing the precautions we have

recommended are taken to prevent losses of fluid before narcosis is complete.

#### Biochemical Considerations.

The particular interest for us in these findings has already been explained. Reliable basal figures in human beings are more difficult to obtain on account of the added effects of fear and premedication, both of which can change the levels of these metabolic indices. More reliable physiological and biochemical observations can be made on dogs, where the primary effect on blood levels of the anaesthetic can be accurately foretold.

**Acid Base Metabolism.** It is now generally accepted that inhalation anaesthetics bring on at once a decided rise in the hydrogen ion concentration of the blood, an effect which is rapidly heightened by operative shock. In certain patients, for example, nephritics, diabetics *et cetera*, when a fall in the acid base balance already exists, the advantages of an anaesthesia unaccompanied by such a change will be undisputed. A study of "Avertin" in this regard shows us that during anaesthesia there is no appreciable fall in the plasma carbon dioxide combining power, for example, in nephritis. Certainly a slight postanesthetic fall occurred in some cases within three or four hours. This was not the rule, however, and in no instance was any pronounced depression seen exceeding 10% and the most severely nephritic dog was in no way adversely affected.

These findings are in distinct contrast to the statement of Wymer<sup>(16)</sup> who emphasizes the danger of acid intoxication following "Avertin" anaesthesia. The slow and shallow respirations observed with this anaesthetic probably have their biochemical counterpart in the above findings. In other words, there is missing here the acidosis stimulating the respiratory centre, as in the case of the inhalation narcotics.

**Carbohydrate Metabolism.** As regards blood sugar, the usual immediate rise is evident at once after injection, but is distinctly lower than with inhalation anaesthetics. It fell again soon afterwards and remained within normal limits throughout the entire postoperative period in all animals observed.

**Inorganic Phosphates of the Plasma.** The particular interest in inorganic phosphates of the plasma lay in comparing them with those already published<sup>(2)</sup> for the inhalation anaesthetics. Briefly it was found that for these latter a fall occurred if the anaesthetic was satisfactory, whereas a definite and progressive rise was seen in a complicated anaesthesia (*vide* Charts VI and VII).

With "Avertin" there is usually a slight fall in the phosphate level immediately after induction, coincident with the rise in blood sugar. The concentration, however, soon returns to normal or even rises slightly towards the end of the anaesthetic and during the recovery period. When, under a large dose, the anaesthesia is considerably prolonged, a

more distinct rise occurs late in the narcosis, a rise which is probably comparable to that occurring with asphyxia during anaesthesia by inhalation (*vide* Charts I and VII).

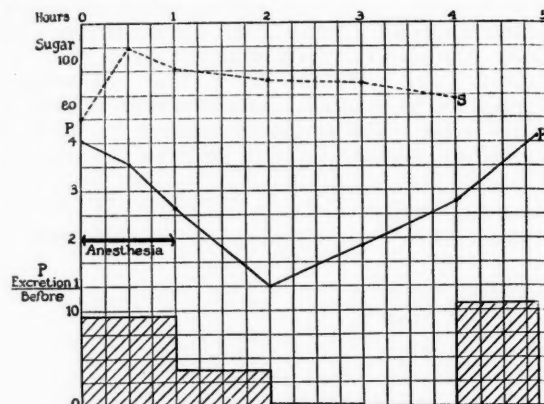


CHART VI.

Uncomplicated ether anaesthesia in a normal dog. P = inorganic phosphate of the plasma in milligrammes per centum. S = blood sugar in milligrammes per centum. Shaded areas indicate milligrammes urinary phosphates excreted per hour. (From *The Journal of Biological Chemistry*.<sup>(2)</sup>)

**Urinary Phosphates.** Urinary phosphates were estimated in three cases. The changes are by no means pronounced, as in uncomplicated inhalation anaesthesia (Chart VI). Nevertheless, immediately

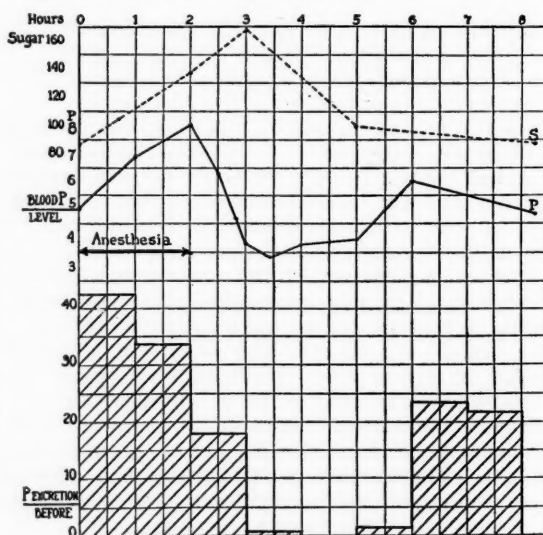


CHART VII.

Complicated ether anaesthesia in a normal dog. P = inorganic phosphate of the plasma in milligrammes per centum. S = blood sugar in milligrammes per centum. Shaded areas indicate milligrammes urinary phosphates excreted per hour. Compare with Charts IV, V and VI. (From *The Journal of Biological Chemistry*.<sup>(2)</sup>)

after induction a moderate and fleeting fall does occur, corresponding to that observed in the blood. Similarly, with raised blood phosphate there is an increased output of these salts in the urine, similar

again to that seen with the inhalation narcotics. The significance of these changes in blood and urine phosphate is by no means clear. In inhalation anaesthesia they were found to be connected with carbohydrate metabolism to a large extent.<sup>(2)</sup>

**Blood Cholesterol.** Mahler has shown for the inhalation anaesthetics that there is a slow rise in the blood cholesterol concentration. We observed a similar change under "Avertin" anaesthesia when this component was sought for. Thus in the dog with advanced nephritis a moderate hypercholesterolemia due to its disease was already present. Under "Avertin" anaesthesia no great change was seen. It seems that "Avertin" does not derange the lipid metabolism further than ether does, even when this has already undergone a change, as indicated by the cholesterol content of the blood.

Dogs deprived of their pancreases were not made use of in this inquiry, as it was thought that the small variations did not justify the large amount of preparatory work required.

#### *"Avertin" Anaesthesia in Renal Insufficiency.*

Contrary to the statements in the literature, renal insufficiency was not found to be an actual contraindication to "Avertin" anaesthesia. In dealing with advanced renal insufficiency we found it advisable to diminish the dosage slightly, for example, from 5% to 10%. This reduced tolerance we are rather inclined to attribute to lowered resistance in general than to the diminished renal insufficiency, as it does occur also with inhalation anaesthetics. The detoxication takes place in other organs.

No experiments were performed on dogs with liver insufficiency. Normal dogs after repeated and potent doses of "Avertin" yielded no evidence of recent acute hepatic damage, as is easily obtained by chloroform anaesthesia.

#### *"Sodium Amytal."*

Like "Avertin" "Sodium amytal" displayed similar or even more pronounced advantages over inhalation anaesthesia. After the administration of an adequate dose of the anaesthetic no further attention to the narcosis was necessary throughout an operation lasting an hour or more. The biochemical changes are even less pronounced than with "Avertin." The changes in the blood sugar are practically negligible and on no occasion has an appreciable fall in the carbon dioxide combining power of the plasma been observed. During prolonged anaesthesia the plasma phosphates show a rise which in all probability rests on a similar basis to that seen with "Avertin." The contrast between the usual inhalation anaesthetics, chloroform, ether, on one hand, and the "injection" anaesthetics ("Avertin," "Amytal") on the other, as demonstrated by their biochemical effects on the blood plasma, surely indicate a fundamental difference between these two types of anaesthesia as regards their mode of action. With "Sodium amytal" these

differences are even more pronounced than with "Avertin."

As far as our work goes, "Sodium amytal" seems to produce just as satisfactory an anaesthesia as does "Avertin" and with a wider margin of safety, at least for dogs and puppies. So far no death due to "Sodium amytal" has been observed in our series. As with man, there is the much prolonged recovery period frequently associated with excitement, a distinct contrast to the rapid recovery from "Avertin." This feature may, of course, be disadvantageous or otherwise, according to the nature of the experimental work for which the anaesthetic is required. The prolonged period of recovery following "Sodium amytal" may be somewhat shortened by the use of the so-called antidote, ephedrine sulphate and caffeine sodium benzoate.

On the whole we would prefer "Sodium amytal" rather than "Avertin" for routine laboratory work, except when intravenous injection becomes technically too difficult or a rapid uncomplicated recovery is desired.

With such anaesthetics as "Sodium amytal" and "Avertin" which are not administered and excreted by the respiratory route, the liver and kidneys have to be considered as the alternative organs of excretion which have the additional property of detoxication. Renal insufficiency seems to be of minor influence in "Avertin" narcosis and its sequelae. The process of detoxication which most probably takes place in the liver, does not seem to be much affected even by severe renal insufficiency and the dosage required and tolerated by nephritic animals is only slightly smaller than that required and tolerated by the normal dog. So far not much is known of the fate of "Sodium amytal" and of the manner in which the body excretes it. But our experiments with "Sodium amytal" on dogs with renal insufficiency brought out the fact that animals with renal insufficiency require a much smaller dose than normal dogs. This is tentatively explained by the assumption that the "Sodium amytal" is excreted by the kidneys somewhat similarly to such drugs as phenolsulphonephthalein. The renal deficiency delays the commencement of the excretion which in addition is smaller and slower than in the normal animal. In the nephritic animal, compared with the normal one, "Sodium amytal" reaches the nervous centres in a higher concentration and maintains an effective concentration for a longer time. But the general effects of "Sodium amytal" anaesthesia on the nephritic organism, after a proper dose has been given, appear just as favourable as with normal animals. There is even less excitement. So far no deleterious effects on the kidneys have been recognized.

#### *Clinical Significance of These Experiments.*

The results of this experimental investigation enable us to make certain suggestions in regard to its clinical application. To avoid any misunderstanding we should emphasize that the dose of all

anæsthetics, as far as is known, is considerably larger for the dog than for man.

Our observations as regards clinical effects, safety margin *et cetera* run closely parallel to the conclusions which can be drawn from the clinical use of these drugs, regard being paid to the relatively small number of published cases of "Sodium amytal" as compared with "Avertin" anæsthesia.

In neither case does renal insufficiency of reasonable severity appear to be a contraindication to the use of these anæsthetics, although when "Sodium amytal" is used, the usual dose should be reduced in accordance to the degree of insufficiency.

It must be admitted that a large dose of "Avertin" is associated with a small but definite risk, while we were able to use relatively large doses of "Sodium amytal" without disastrous results.

With "Avertin" we have not found that washing out of the bowel is a necessary preliminary.

The prolonged recovery period would serve to render "Sodium amytal" of superior usefulness in the treatment of such conditions as tetanus, strychnine poisoning, rabies, eclampsia, *status epilepticus* and other convulsive disorders, though here there may be a temporary period of increased excitement. Though "Sodium amytal" shortens still further the time of postoperative suffering, patients would still require the constant vigilance of a nurse until full consciousness is regained. The recovery from "Avertin" anæsthesia, on the other hand, is rapid and uncomplicated.

Fewer fears need be entertained that these drugs will contribute to postoperative acid intoxication in nephritis or, probably, *diabetes mellitus* than with the inhalation anæsthetics.

#### ACKNOWLEDGEMENTS.

We should like to express our sincerest thanks to the Sydney representative of Eli Lilly, Limited, for generously donating a quantity of "Sodium amytal."

#### CONCLUSIONS.

1. In "Avertin" and "Sodium amytal" we have valuable additions to the anæsthetics available for the experimental worker.

2. "Avertin" is a reasonably safe and non-toxic anæsthetic, but with human beings the margin of absolute safety is somewhat less than has been claimed by some of the earlier observers. In our series of normal dogs a dose up to 0.48 gramme per kilogram could be given with absolute safety.

3. No untoward results followed even deep and prolonged "Sodium amytal" anæsthesia and we now prefer "Sodium amytal" as being a safer, cleaner and more certain anæsthetic for ordinary experimental use.

4. Renal insufficiency was not found to be a contraindication to the use of "Avertin" and

"Sodium amytal." Smaller doses of "Sodium amytal" should be given in accordance with the degree of renal insufficiency.

5. In contrast to the usual inhalation anæsthetics, "Avertin" given by the rectum and "Sodium amytal" given intravenously have no material influence during anæsthesia on the carbon dioxide combining power of the blood plasma. Occasionally a moderate fall was observed following "Avertin" anæsthesia. Again, after the administration of "Avertin" or "Sodium amytal" no changes in the inorganic phosphates of the blood were observed such as occur following the inhalation narcotics. The small alterations in the blood sugar level, particularly with "Sodium amytal," serve still further to distinguish "injection" anæsthesia from inhalation anæsthesia.

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**"AVERTIN" RECTAL ANÆSTHESIA: EXPERIENCE ABROAD AND AT HOME.<sup>1</sup>**

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As a subject for my presidential address to this society this evening I have endeavoured to select one of new and general interest and have chosen "Avertin" Rectal Anæsthesia: Experience Abroad and At Home."

The first recorded use of the rectal route for administration of anæsthetics was the trial by Roux in 1846 of an aqueous solution of ether. This resulted in injury to the rectal mucous membrane. Later on Pirogoff tried vaporized ether, but this also was useless on account of the damage to the mucosa. In 1913 Gwathmey experimented with a solution of ether in oil with a preliminary administration of morphine and magnesium sulphate, but this method which was also tried in Melbourne, found little favour. Paraldehyde given by the rectum has also been used, but apparently had not much success to recommend it for general acceptance.

To Eichholtz is due the credit of recognizing the valuable properties of "Avertin," the new basal anæsthetic, and introducing it into therapeutics. "Avertin" was first produced by Willstatter and Duisberg by yeast fermentation of bromal, but since then it has been found that it can be produced more easily in other ways. The advent firstly of "Avertin" (crystalline) and later of "Avertin" (fluid) is in my opinion an epoch-making method of rectal anæsthesia. The pharmaceutical scientific department of the I. G. Farben-Industrie of Leverkusen, Germany, was very thorough in its efforts to prove that "Avertin" fulfilled all the necessary requirements for a perfect rectal anæsthetic. Such requirements are:

1. The drug must not be irritant nor damaging to the rectal mucosa.
2. It has to be of sufficiently general therapeutic value to make it widely useful.
3. It must produce a narcosis of not much danger or anxiety.
4. It must be sufficiently potent in safe dosage to produce: (i) full general anæsthesia, (ii) at least a condition of basal anæsthesia or extensive prenarcois, so that only very little additional inhalation anæsthetic is required to cause complete anæsthesia and so lessen the incidence of post-operative vomiting, bronchitis and pneumonia which are very real though often underestimated postinhalation anæsthetic complications.

While in London, at the Middlesex Hospital, I was given a letter of introduction to Professor Hans Finsterer, of Vienna, and was earnestly advised to see his gastric surgery performed under local splanchnic anæsthesia and by good fortune was then

induced by him to see Professor Unger, Surgeon to the Rudolf Virchow Krankenhaus, Berlin, a hospital of 2,500 beds, operate under this new rectal anæsthetic, "Avertin," which he, together with other German surgeon-professors, was trying on behalf of the United Chemical Manufacturers of Germany, known as I. G. Farben. The doctors in charge of the administration were exceedingly kind and obliging and demonstrated the technique and discussed at length the benefits and effects of this method of anæsthesia. They informed me that I was the first non-German doctor to see "Avertin" used and suggested that I apply at the office of the I. G. Farben-Industrie A.G. in the Kurfurstendamm, Berlin, for a supply. The general secretary was sorry that at that time none could possibly be made available for use outside their control, but promised to send to me in Australia some of the first lot released for general use. This they did in August, 1929. One can only but commend the manufacturers for their excellent method of introducing this product to the profession, only after it had been thoroughly tested by anæsthetists and surgeons appointed by them. After the German doctors had tried it, supplies were distributed through the Anæsthetics Committee of the Medical Research Council of Great Britain to several recognized English anæsthetic specialists and when this Committee had reported favourably on its safety and value, it was then made available for general use.

At the time I was in Berlin, the latter end of April, 1927, Professor Unger had then successfully performed over five hundred operations under "Avertin" anæsthesia and the doctors there were very enthusiastic concerning it. Amongst the series of operations that I saw performed under this rectal anæsthesia were such procedures as cholecystectomy for acute cholecystitis with stones and choledcho-duodenostomy in a patient with scirrhus carcinoma of the pancreas. The "Avertin" used at that time was a white crystalline powder, tri-brom-ethyl alcohol ( $\text{CBr}_3 \text{CH}_2\text{OH}$ ), used in a faintly acid 2.5% solution in water and previously known as E 107. The preparation now mostly used is "Avertin" (fluid) in which the "Avertin" is kept stable in solution by the presence of amylene hydrate. In the early days of the experimental period there were a few fatalities due to over-dosage and non-appreciation of the fact that chemical alteration had occurred in the "Avertin" administered. The strength of the solutions I saw used in Berlin were: For very frail people, 0.1 gramme per kilogram (body weight); for slight people, 0.125 to 0.15 gramme per kilogram; for stout people, 0.175 gramme per kilogram; for alcoholics, 0.2 gramme per kilogram. Narcosis was effected in four to eight minutes, the patients just falling off to sleep. There was no excitation and respiration was even and quiet. They had experienced no case of rectal inflammation and post-operative vomiting; pain and lung complications were conspicuous by their absence. The patient's

<sup>1</sup>Read at the Annual Meeting of the Victorian Medical Women's Society, on March 10, 1930.

colour went a little purplish or bluish during the narcosis and the blood pressure used to fall ten to thirty millimetres of mercury. After the operation the patients had an "all-out" appearance, but the doctors were well satisfied with the success of the drug. After return to bed the patients usually slept for one or more hours and care was taken to see that the jaw did not sag and impede respiration until the tone returned. A small dose of barbitone was given on the evening prior to operation and morphine 0.02 gramme (one-third of a grain) twenty minutes before operation. Some patients needed during the operation a little ether or nitrous oxide. The use of "Avertin" was debated at a Berlin medical conference which was being held at that time.

So much for my early personal observation of its use in Berlin in 1927.

After a very satisfactory trial and report by its German medical advisers, twenty thousand operations, I understand, having been done under it, the I. G. Farben-Industrie made "Avertin" available for clinical trial in Great Britain under the aegis of the Anaesthetics Committee of the Medical Research Council and a report from this Council, entitled "The Use of Avertin in Anaesthesia," by Dr. J. Blomfield, of Saint George's Hospital, London, and Dr. F. E. Shipway, of Guy's Hospital, London, was published in *The Lancet* in March, 1929.

This subject was further discussed in the Section of Anaesthetics of the Royal Society of Medicine in November, 1929. Their report was based on a wide range of operations, about two hundred in number, on patients who were the subjects of very varied surgical conditions and who were of varied ages and states of health. The operations covered a wide surgical field, from simple ligature for hemorrhoids to laryngectomy, gastrostomy, hysterectomy and thyroidectomy. There were fatalities in two cases, the patients being very bad subjects for operation and anaesthesia. In one instance the "Avertin" was held to be blameless and in the second the "Avertin" may have been a contributing factor.

#### Chemical Properties of "Avertin."

"Avertin," as previously stated, is a tri-brom-ethyl alcohol,  $\text{CBr}_3 \text{CH}_2\text{OH}$ , a crystalline white powder, soluble in water with difficulty. "Avertin" (fluid) is a solution made stable by amylene hydrate. The solid "Avertin" is an easily sublimating substance with a melting point of  $79^\circ$  to  $80^\circ \text{C}$ . It tends to be decomposed by light and air. The solution for injection is made 3% in distilled water at a temperature of  $40^\circ \text{C}$ . and the temperature must not be allowed to fall below  $35^\circ \text{C}$ . If allowed to cool, the "Avertin" crystallizes out and if it is heated above  $42^\circ \text{C}$ ., some decomposition may take place and hydrobromic acid is formed together with dibrom-acetaldehyde, which even in small amounts causes intestinal injury. In practice the Congo red test

soon proves whether any decomposition has occurred and so completely prevents the possibility of danger of using an impure liquid. The universal experience and my own is that "Avertin" neither injures nor irritates the rectal mucosa.

For the Congo red test 0.02 mil (two minims) of Congo red solution, one in one thousand, are mixed in 3.9 mil (eighty-five minims) of the solution prepared for injection and the colour must remain orange red. A blue colour indicates dangerous decomposition.

#### Procedure for Administration.

An effective aperient is given the morning of the day before operation. The German anaesthetists in almost all cases give veronal or a similar drug on the evening preceding operation. The British workers consistently refrain from this. They find no need for this extra sedative and rely on a routine morphine-atropine, morphine-scopolamine or "Omnopon" injection given one to one and a half hours prior to the time of operation. It is thought that this allows a lesser amount of "Avertin" to be effective. In my own work I have given morphine 0.01 gramme (one-sixth of a grain) as a routine, three-quarters to one hour before the administration. The rectum should be washed out on the evening previous to operation and it is not advisable to repeat this. Five to ten minutes are taken for the 3% solution of "Avertin" in distilled water at  $40^\circ \text{C}$ . (previously submitted to the Congo red test) to be run into the rectum through a soft rubber tube or catheter which must be introduced ten centimetres (four inches) or more beyond the anus. The enema apparatus (which consists of a glass funnel or a Ramsay's "Thermos" flask, with rubber tubing and catheter) should be previously warmed in hot water in order to maintain the temperature of the solution. During the period of anaesthesia attention to the preservation of the airway is necessary in case the tongue or jaw sags back.

#### Dosage.

In the cases I saw in Berlin the dosage was as previously stated from 0.1 to 0.2 gramme per kilogram body weight. The British recommendation is for a slightly less scale, 0.09 to 0.15 gramme per kilogram body weight. J. Blomfield, except in his first few cases, used 0.02 gramme (one-third of a grain) of "Omnopon" and then 0.1 gramme per kilogram and the evidence shows this to be a safe procedure; approximately 33% of the patients required no other anaesthetic. In the remainder the drug had to be supplemented by a little ether. The necessity for supplementary inhalation anaesthetic arises less frequently with doses of 0.13 to 0.15 gramme per kilogram body weight. The question of correct dosage for each patient is a little difficult. The body weight, as the sole guide to the dosage, is not quite accurate, for it is well known that different patients react differently to narcotics, while different temperaments and different states of

bodily vitality play a part in dosage estimation, as well as body weight. Nevertheless the body weight *plus* personal experience with the various types of patients gives a reliable guide within the dosage range of 0.09 to 0.15 gramme per kilogram body weight to the amount of "Avertin" necessary to provide a good induction of narcosis. This may be: (i) Just sufficient alone for surgical anaesthesia or (ii) an excellent basal anaesthesia which, supplemented by a comparatively small amount of inhalation anaesthetic, provides a perfectly satisfactory surgical anaesthesia.

The supplementary inhalation anaesthetics which may be used are: (i) Gas and oxygen, (ii) ether, (iii) chloroform-ether mixture. I myself have found very satisfactory results with a mixture of one part of chloroform and five parts of ether.

#### Clinical Effects of the Injected Solution.

The "Avertin" is rapidly and completely absorbed by the bowel and symptoms of narcosis are produced in a few minutes. In my experience the patient is drowsy and languid in two to four minutes and sound asleep in four to eight minutes. The period of unconsciousness varies from two to four hours as a rule. The British report states that in forty-five minutes all the "Avertin" has left the bowel. The unconsciousness which resembles deep sleep, is produced quickly and quietly without excitement or any unpleasant sensation. In up to fifteen minutes the conjunctival reflex is absent and the corneal reflex also as a rule. The pupil is small and reacts to light. Muscular relaxation is profound as in sleep. Respiration is regular and easy and in some cases slow and shallow. I have noticed that opening the peritoneum, traction on the peritoneum, traction on the appendiceal mesentery and on the gall bladder and cutting or suturing in the region covered by the pubic hair temporarily increased the respiratory rate and excursion. The blood pressure falls ten to thirty millimetres of mercury, the fall being greater in proportion to the dosage strength of "Avertin." The pulse rate in my patients showed remarkably little alteration, except in a radical breast operation at the time of the actual removal of the breast, when the pulse volume decreased, but was immediately restored by the administration of 0.5 cubic centimetres of "Pituitrin." The colour may remain normal if the airway is kept clear. The patients seen in Berlin with the larger scale of dosage had a faint bluish-purple tint. In my cases some patients stayed normal, others had the bluish, faintly cyanotic tint. In half to three-quarters of an hour the patient is put on the operating table and has all the appearances of being fully anaesthetized. In my later cases I have administered the "Avertin" enema on the operating table and the operation can be commenced in twenty to twenty-five minutes. If the narcosis is just below the degree of full surgical anaesthesia, the fact may be detected by pricking with the towel clips to elicit faint reflex movements or by applying

an open mask, well moistened with ether, close to the mouth. If the respiration does not alter from the irritation of the ether vapour on the pharynx, the operation can be commenced. If the narcosis is not quite surgical, a few drops of one in six chloroform-ether mixture will soon produce the required depth of anaesthesia. No untoward effects of the "Avertin" on respiration or circulation have been reported or found in my own cases. Blood pressure does not fall more than thirty millimetres, unless the severity of the surgical procedure is great. The respiratory stimulant, carbon dioxide or lobeline, or the circulatory stimulant, one or two cubic centimetres of a 5% solution of ephedrine, would most likely be required. The foregoing is the picture of most cases of "Avertin" anaesthesia, the exception being provided by alcoholic patients in whom the "Avertin" stupifies and a relatively large amount of inhalation anaesthetic anaesthetizes. Nevertheless, the patient will remember nothing after the rectal administration.

#### Recovery Period.

The patient after return to bed is unconscious as if in sleep, for a varying period of one to three hours which is followed by a dozing and waking period. During both these periods the corneal reflex is present and violent stimulation can break into this sleep, so that the fear of foreign matter entering the larynx without being reflexly ejected is no more than in ordinary anaesthesia. A large number of patients treated by one surgeon with diathermic coagulation for extensive carcinoma of tongue and tonsil favourably establishes this point (Mr. Morrin, *The Lancet*, March, 1929). The remarkable after effect is the length of the period of retrospect amnesia and analgesia which carries the patient over the time when the postoperative pain is usually severe, namely, the first two or three days. The whole process, from the administration of the enema onwards, is like exaggerated sleep. During the first twenty-four or thirty-six hours the patient is more sleepy than awake; during the next twenty-four hours is more awake than sleepy. On the third day, aperiens day, there is just a little uncomfortable feeling until the bowels act. On the fourth, fifth and sixth days the patient experiences a feeling of restfulness and on the seventh day is quite alert and there is that total absence of retrospect fear which is more or less the dreaded memory of patients operated upon under ordinary inhalation anaesthesia. This presents the average picture, but probably mild variations would be noted, according to the temperament of the patient.

In the great majority of cases the freedom from severe pain and the absence of violent vomiting or retching, nausea and abdominal distension or excessive flatulence, as well as of lung complications, are very real advantages to the patient and to the abdominal wound, if any. Indeed there is a notable absence of any nausea to food and the early opening of the bowels is quite easy. Some patients experience rather a definite feeling of postoperative well

TABLE SHOWING RESULTS

Number, Sex, and Age of Patient in Years.	Pre-Operative General Condition.	Surgical Condition.	Operation Performed.	Pre-Narcosis.	"Avertin" Dosage.	Administered.	Narcosis Established.	Operation Commenced.
1 M. 65	Weight, 74.7 kilograms (11 stone 12 pounds), nervous temperament, losing weight, alcohol always, early debility.	Carcinoma of upper end of oesophagus	Gastrostomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.1 gramme per kilogram body weight.	In bed.	In six minutes.	One hour after administration.
2 F. 65	Thin, wiry, parchment-like skin.	Stomach hour-glassed by adhesion band; chronic cholecystitis.	Removal of adhesions, cholecystectomy, appendectomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one and half hours before.	0.1 gramme per kilogram body weight.	In bed.	In five minutes.	Fifty minutes after administration.
3 M. 66½	Vomiting all food for two weeks; loss of flesh; big frame.	Pyloric carcinoma, extensive involvement of stomach, <i>et cetera</i> .	Jejunostomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.1 gramme per kilogram body weight.	In bed.	In seven minutes.	One hour after administration.
4 F. 30	Weight, 45 kilograms (7 stone 2 pounds). Frail, anemic.	Polypoid endometritis and myomata.	Hysterectomy, appendectomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.1 gramme per kilogram body weight.	In bed.	In six minutes.	One hour after administration.
5 F. 47	Robust.	Cord-like perigastric adhesion, gall bladder and duodenum adherent, cystic duct sacculated.	Removal of adhesions, cholecystectomy, appendectomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.125 gramme per kilogram body weight.	On operating table.	In five minutes.	One hour after administration.
6 F. 16	Weight, 45.9 kilograms (7 stone 4 pounds). Good.	Acutely retroposed and retroflexed uterus; chronic appendicitis.	Dilatation and curettage, appendectomy, Gilliam's operation.	0.008 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.11 gramme per kilogram body weight.	In bed.	Sleep in two and a half minutes, narcosis in four minutes.	Twenty-five minutes after administration.
7 F. 51	Weight, 61.6 kilograms (9 stone 11 pounds). Good.	Adhesions of whole of under surface (right) of liver to duodenum and transverse colon.	Adhesions separated, bowel freed, cholecystectomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.125 gramme per kilogram body weight.	On table.	Sleep in three minutes, narcosis in six minutes.	Thirty minutes after administration.
8 F. 31	Anæmic; general condition fair.	Plastic perihepatitis, broad gastro-colic, omental adhesion to gall bladder and duodenum, chronic cholecystitis.	Adhesions removed, cholecystectomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.125 gramme per kilogram body weight.	On table.	Sleepy in four minutes, narcosis in seven minutes.	Thirty minutes after administration.
9 F. 49	Weight, 72 kilograms (11 stone 6 pounds). Good.	Carcinoma of right breast.	Radical operation, with removal of <i>pectorales</i> , major and minor.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, one hour before.	0.125 gramme per kilogram body weight.	In bed.	Sleepy in three minutes, narcosis in seven minutes.	Twenty-five minutes after administration.
10 F. 38	Weight, 59 kilograms (9 stone 5 pounds). Good.	Chronic appendicitis, retroverted uterus, lacerated cervix.	Trachelorrhaphy, appendectomy, Gilliam's operation.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, three-quarter hour before.	0.125 gramme per kilogram body weight.	On table.	Sleepy in four minutes, narcosis in six minutes.	Twenty minutes after administration.
11 F. 39	Weight, 67 kilograms (10 stone 9 pounds). Good.	Multiple myomata, chronic appendicitis, adherent to peritoneum over iliac vein.	Appendectomy, sub-total hysterectomy.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, three-quarter hour before.	0.125 gramme per kilogram body weight.	On table.	In five minutes.	Twenty minutes after administration.
12 M. 59	Weight, 78.7 kilograms (12 stone 7 pounds). Fairly good.	Enlarged prostate.	Second stage removal.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, three-quarter hour before.	0.12 gramme per kilogram body weight.	On table.	In six minutes.	Twenty minutes after administration.
13 F. 44	Weight, 60.3 kilograms (11 stone). Fair.	Left subphrenic tumour with ascites.	Exploratory operation for sarcoma of the spleen.	0.01 gramme ( $\frac{1}{8}$ grain) morphine, three-quarter hour before.	0.125 gramme per kilogram body weight.	On table.	In seven minutes.	Twenty minutes after administration.

## OF "AVERTIN" NARCOSIS.

Supplementary Inhalation.	Pulse.	Respiratory.	Vomiting.	Pain.	Discomfort.	Remarks.
24 cubic centimetres (6 fluid drachms) chloroform-ether mixture.	Practically no variation.	Respirations easy and free; faint cyanotic tint of face.	None.	None.	None.	Talked with his friends re business during the afternoon without any remembrance of doing so. Woke at 6 p.m. and asked the nurse when the operation was to be.
12 cubic centimetres (3 fluid drachms) ether at the end as stimulant.	Slowed.	Cold face; respirations very slow and shallow; very faintly cyanotic.	Two lots of 60 cubic centimetres (2 ounces) clear (fluid) each.	None.	None.	Awoke one hour after return to bed. Slept all afternoon. At 6 p.m. asked nurse to hurry the doctor to come and do the operation.
8 cubic centimetres (2 fluid drachms) chloroform-ether mixture.	No variation.	Cold face, cyanotic tint.	Black (obstructive) vomiting.	Moderately, severe over wound.		Died twenty-one hours after operation.
24 cubic centimetres (6 fluid drachms) ether.	Pulse, loss of volume and force.	Face cold, no colour change.	Two small lots of clear fluid.	None.	None.	Remembers no discomfort of operation.
20 cubic centimetres (5 fluid drachms) chloroform-ether mixture.	96 pulse at start, 84 at finish.	Reddish-purple tint.	None.	None.	None.	Said she left hospital without feeling that she had undergone an operation.
32 cubic centimetres (8 fluid drachms) chloroform-ether mixture.	No change.	No change in colour; respirations easy as in sleep.	None.	None.	None.	No remembrance of the first twenty-four hours after the operation. Quite delighted with her condition and experience as compared with that of similar operation case in same ward.
8 cubic centimetres (2 fluid drachms) chloroform-ether mixture for the horse-hair sutures.	No change.	Slight increase in natural florid colour.	None.	None.	None.	Very pleased.
14 cubic centimetres (3½ fluid drachms) chloroform-ether mixture.	No change.	No colour change.	None.	None.	None.	Says very different experience to previous operation. (Appendicectomy + Gilliam's operation.)
48 cubic centimetres (12 fluid drachms) chloroform-ether mixture when baring the chest wall.	Pulse lost force and volume while removing the pectorals.	Cyanotic tint.	None.	None.	None.	No pain with any dressing. Using arm freely in three days.
64 cubic centimetres (16 fluid drachms) chloroform-ether mixture.	No change.	No change.	Vomited 60 cubic centimetres (2 ounces) clear fluid three times after a drink.	No pain.	Slight feeling of discomfort.	Does not remember anything of the first twenty-four hours after the operation.
A little chloroform-ether mixture.	No change.	No change.	None.	None.	None.	The absence of vomiting or discomfort and the fact that she slept peacefully all night worried the night-sister, whose first "Avertin" case this was.
Nil.	No change.	No change; increased excursion at time of removal.	None.	Feeling of pressure over bladder; later, for two days had bouts of intense rhythmic spasms of pain.	Required several lots of morphia.	Sleepily awake two hours after operation. Speaking and fairly awake five hours after.
8 cubic centimetres (2 fluid drachms) chloroform-ether mixture.	No change.	No colour change; respiratory excursions deepened while exploring the spleen.	No.	No pain.	None.	Remarkably comfortable and easy post-operative convalescence.

TABLE SHOWING RESULTS OF

Number, Sex, and Age of Patient in Years.	Pre-Operative General Condition.	Surgical Condition.	Operation Performed.	Pre-Narcosis.	"Avertin" Dosage.	Administered.	Narcosis Established.	Operation Commenced.
14 F. 21	Weight, 58.9 kilograms (9 stone 5 pounds). Good.	Subacute appendicitis.	Appendicectomy.	0.01 gramme ( $\frac{1}{10}$ grain) morphine, one hour before.	0.125 gramme per kilogram body weight.	On table.	In five minutes.	Fifteen minutes after administration.
15 F. 21	Weight, 49.9 kilograms (7 stone 13 pounds). Good.	Chronic appendicitis.	Appendicectomy.	0.01 gramme ( $\frac{1}{10}$ grain) morphine, three-quarter hour before.	0.11 gramme per kilogram body weight.	On table.	Sleepy in four minutes, narcosis in six minutes.	Twenty minutes after administration.
16 M. 75	Weight, 63.9 kilograms (10 stone 2 pounds). Fair for his age; losing weight for six months; has weakened since this attack.	Acute cholecystitis, dilated gall bladder with small stones.	Cholecystectomy.	0.01 gramme ( $\frac{1}{10}$ grain) morphine and 0.26 milligramme ( $\frac{1}{250}$ grain) atropine, one and a half hours before.	0.10 gramme per kilogram body weight.	On table.	Intwelve minutes.	Thirty minutes after administration.

being. In my own patients preoperative and post-operative excitement was quite absent.

#### Elimination of "Avertin."

"Avertin" has been shown to be eliminated by the liver and kidneys in combination with glycuronic acid. The conclusions in the report on the pharmacological aspects of "Avertin" (*The British Medical Journal*, October 19, 1929) by F. B. Parsons, of the Pharmacological Laboratory, Cambridge, state that in both man and animals "Avertin" is excreted in the urine over a period of several days, considerably more than 50% being excreted in the first twenty-four hours. Practically all the "Avertin" was excreted in forty-eight hours with traces up to the sixth day.

#### Contraindications for "Avertin."

Advanced rectal disease, serious diseases of the liver or kidneys, operative procedures in which a rapid fall of blood pressure or a gross loss of blood is to be expected, form the only contraindications for its use. There is no contraindication on the score of age or state of bodily health, cachexia and debility included, but here cautious dosage is recommended. Professor Unger reports the anaesthetization with "Avertin" of patients with pronounced jaundice without ill effect.

#### Special Indications.

The Anaesthetics Committee report states that "Avertin" has a special value for: (i) Patients who dread the anaesthetic; (ii) patients who have suffered after former inhalation anaesthetics; (iii) subjects of exophthalmic goitre; (iv) cases in which the psychic aspect of the matter is of vital import; (v) patients needing long operations which do not require very deep anaesthesia, for example, long operations on bones, plastic operations and laryngectomy; (vi) injections for trigeminal operations;

(vii) patients with pulmonary complaints; (viii) prolonged operations about the head and neck.

My personal experience with the use of "Avertin" will probably be rendered more lucid by a tabulated list of cases with essential notes thereon. These are sixteen patients from the private practice of myself and my husband, Dr. T. A. Wright, upon whom we have operated under "Avertin" anaesthesia since the middle of December, 1929. In each instance one of us has personally administered the "Avertin" and an anaesthetist has always been present to administer any necessary supplementary inhalation anaesthetic.

#### Supplementary Notes of Cases.

The pulse rate under "Avertin" anaesthesia is remarkably little altered and by "no change" in the tabulated list is meant no alteration in rate within a range of four beats per minute above or below preoperative rate and no appreciable alteration in volume and force.

The supplementary anaesthetic used is a mixture of chloroform, one part, with ether, five parts, and its use is only required now and again for a few minutes at a time during the operation to quieten occasional reflex movements caused by traction on peritoneum, caecum and appendix or by suturing of the peritoneum and skin edges.

The anaesthesia and relaxation were perfect in all cases and for upper abdominal work respiratory heaving was pleasantly absent. The preoperative and postoperative conditions of the patient were satisfying and free from any anxiety and in no case was any trouble experienced with flatulence or in getting bowels to act. The optimum dosage, except in frail people, I have decided is 0.125 gramme per kilogram body weight and I think the skin and peritoneal reflexes are less in evidence and that less supplementary anaesthetic is required if the opera-

## "AVERTIN" NARCOSIS (Continued).

Supplementary Inhalation.	Pulse.	Respiratory.	Vomiting.	Pain.	Discomfort.	Remarks.
	No change.	No colour change.	Vomited one mouthful of bile without any retching; no further nausea.	Very slight and occasional.	Practically none.	This patient has an enlarged thyroid and, although of querulous temperament, has no retrospect fear or complaint of any discomforts of her operation.
cubic centimetres (fluid drachms) morphine-ether mixture.	No change.	No colour change; increased respiratory excursions while traction on caecum and also on the peritoneum during sewing up.	Nil.	Very slight and occasional.	Practically none.	
cubic centimetres (fluid drachms) morphine-ether	76 in bed, 92 during operation, 84 at finish.	No cyanotic tint; respiration easy and free.	Nil.	Nil.	Nil.	Slept quietly for about four hours, then awoke but somnolent. Slept peacefully all night. Enjoyed tea and toast next morning. Very happy and comfortable; looks very well.

tion be commenced three-quarters to one hour after the administration of the "Avertin" enema.

The slight restlessness at the postoperative period of transition from the more somnolent to the more awakening stage is more apparent in young and virile patients than in the elderly and one injection of morphine 0.01 gramme (one-sixth of a grain) in some cases was all that was necessary for complete postoperative placidity. Others needed no postoperative sedative whatever.

A routine rectal injection of saline solution is given, as usual, on return to bed and 0.5 cubic centimetre of "Pituitrin," followed later by 2.2 milligrammes (one-thirtieth of a grain) of strychnine, is given to the older patients, also as a routine. The younger patients do quite well without these stimulants.

## Conclusions.

"Avertin" is a very valuable addition to the drugs available for the use of the anaesthetist. Its administration should not be left to the nurses, but if it is used with proper care and in moderate dosage under medical supervision, its real and great benefit can be taken advantage of with perfect safety.

## Reports of Cases.

## PARATYPHOSUS A IN AUSTRALIA.

By FRANK L. APPERLY, M.A., D.Sc., M.D.,  
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AND

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BEFORE the Great War paratyphoid fever, due to *Bacillus paratyphosus* A, though fairly common in India, was rare elsewhere, but during the war it appeared in Gallipoli

and France. No proved case, however, has, so far as we are aware, ever been recorded in Australia. The following case is therefore of interest and raises the important question of the source of infection.

The patient was a medical man from another State, aged thirty-five years, who had not been out of Australia. He stated that about three months previously he began to feel tired and miserable, with a distended caecum and some tenderness in the right iliac fossa, but that physical examination revealed nothing more. A month later the pains increased and a tentative diagnosis of chronic appendicitis was made by a colleague. A month after that he complained of headache, photophobia, vertigo, severe epistaxis and a temperature of 39.4° C. (103° F.), from which a diagnosis of influenza was made. After this all soreness and symptoms disappeared, but he often had temperatures of 37.8° to 39.4° C. (100° to 103° F.). A Widal test, made in his own State, yielded no reaction. In spite of the above ill health he attended the Medical Congress.

When first seen by us, the patient had a pulse rate of 102, respiration rate of 27 and temperature of 39.4° C. (103° F.). Apart from the usual characteristics of fever there were no physical signs. The stools were formed and very offensive.

The patient made an uninterrupted recovery, with steadily falling temperature and pulse which reached normal figures after about fourteen days.

The following special examinations were carried out:

1. The blood was examined on admission. The leucocyte count was 9,400 cells per cubic millimetre with the following differential count:

Neutrophile staff forms	4.00%
Neutrophile polymorphonuclear forms	77.50%
Eosinophile cells	0.25%
Basophile cells	0.50%
Lymphocytes	7.50%
Transitional cells	3.25%
Large mononuclear cells	7.00%

Four hundred cells were counted.

2. Macroscopical agglutination of the patient's serum was carried out against emulsion of *Bacillus typhosus*, *Bacillus paratyphosus* A and *Bacillus paratyphosus* B failed to give a reaction. The reading was made after four hours' incubation at 55° C. and again on the following morning. This test was made on admission to hospital.

3. A blood culture taken three days after admission gave a growth next day of a motile Gram-negative bacillus which gave the fermentation reactions of a *Bacillus paratyphosus*. Agglutination of the

first subculture was complete to paratyphoid A serum in a dilution of only one in 400. On third subculture the agglutination was as follows: *Bacillus typhosus* serum one in 40, *Bacillus paratyphosus* A serum one in 10,400, *Bacillus paratyphosus* B serum one in 40.

The patient's serum agglutinated the organism in a dilution of one in 80.

Dr. W. Sawers, of the Commonwealth Serum Laboratories, and Dr. Lucy Bryce and Miss F. E. Williams, of the Walter and Eliza Hall Institute of Research, Melbourne, kindly extended the fermentation tests and carried out agglutination tests, all of which confirmed the identification of the organism as *Bacillus paratyphosus* A.

4. The serum of the patient eight weeks after the illness was found to give only a partial agglutination in a dilution of one in 30 against two strains of *Bacillus paratyphosus* A and also against the patient's own organism.

Our next endeavour was to trace the source of the infection. The patient stated that a week before he began to feel unwell, that is, about thirteen weeks before he was seen by us, he had attended a girl with typical typhoid fever. She became steadily worse and died of meningitis. Her serum was not examined. Attempts to trace her infection further were fruitless.

## Reviews.

### PROGRESS IN DISEASES OF THE EYE, EAR, NOSE AND THROAT.

THE "Practical Medicine Series" comprises eight volumes on the year's progress in medicine and surgery. The volume under review deals with the year's contributions in the department of eye, ear, nose and throat. It is the combined work of three editors, Dr. Small, Dr. Andrews and Dr. Shambaugh, of Chicago. It is an excellent volume and is quite up to the standard of its many predecessors. Two-thirds of the book are devoted to diseases of the ear, nose and throat.

Moving pictures have at last come to take their place in the teaching of ophthalmic surgery. Charles Shannon explains the technique and tells of the difficulties met with in introducing the new method of instruction at Jefferson College. They employ a Bell-Howell camera (sixteen millimetre) with a speed of sixteen pictures per second. A Kirby spot-light and a hammer hand lamp supply the illumination.

One page is given to the researches of Noguchi into the ætiology of trachoma, a subject of great interest to Australia, where trachoma is still far too common. Noguchi, working in West Africa, discovered a new bacterium, the *Bacterium granulosis*, in human trachoma. He conveyed the disease to monkeys and carried the infection through five generations. The editors conclude that the ætiological agent of trachoma has at last been discovered.

In the discussion on the principles of treatment in corneal ulceration the views of Temple Smith, published in THE MEDICAL JOURNAL OF AUSTRALIA, are mentioned. A paper by the same author from *The British Medical Journal* on optic neuritis and dental sepsis is quoted freely.

Delayed corneal ulceration from mustard gas is one of the most unpleasant aftermaths of the war to those affected. Those who saw the severe types of this disease shown at the clinical meeting in Sydney at the Australasian Medical Congress (British Medical Association) last September, will read with interest the description here given.

*Herpes zoster ophthalmicus* is given at some length and an interesting development is the treatment of a patient

with convalescent serum from another person recently affected. Eleven days after the onset of the disease the patient was given an intramuscular injection of 8.5 cubic centimetres of the blood serum of another patient who six weeks before had recovered from a severe attack of perineal *herpes zoster*. The symptoms cleared rapidly with the exception of the iritis; only one injection appears to have been given.

The absence of any reference to slit-lamp work is a notable omission in this year's annual. The chapters on ophthalmic therapeutics and new instruments are very short and contain little of interest. Protein therapy is discussed at some length. It is still very much on trial, but seems of most benefit in cases of iritis, irido-cyclitis and for the prevention of the uveitis of sympathetic ophthalmia.

The section dealing with the ear is the smallest section of the book. Pitman believes that the hypertrophied tonsil causes ear disease by keeping the Eustachian tube unduly open. This would explain the readiness with which children can inflate their tubes and ears and their proneness to Eustachian tympanic catarrh. Fifty acute middle ear infections in man were studied bacteriologically by Fischer. *Streptococcus hemolyticus* was the commonest organism found, while staphylococcus and pneumococcus were next in frequency. The subject of facial paralysis associated with acute *otitis media* is of interest. It is an uncommon occurrence; available statistics record less than 1% of infections in all otitic suppurations. Most of the infections are of peripheral origin and are characterized by a compressive factor, such as congestion, hæmorrhage or exudate within the nerve sheath. Prognosis is good, though recovery may be very slow.

Paralysis of the sixth nerve instead of the seventh may occur in *otitis media* and is of interest to ophthalmic surgeons. Seven cases were reported by Boonacker. They occur in acute rather than in chronic *otitis media*. In this connexion must be mentioned Gradenigo's syndrome. This consists of acute *otitis media*, sixth nerve paralysis and severe parieto-temporal pain. This syndrome indicates leptomeningitis as a complication of the ear disease and, should it become diffuse, it is generally fatal.

Chronic deafness which has been a reproach to aural surgery, is treated at some length. Treatment should be preventive rather than curative and much of it lies in the hands of the general practitioner. Removal of enlarged tonsils and adenoids, treatment of nasal catarrh with coryzal vaccines and proper control of swimming and diving in children, indicate the path alike of prevention and progress.

Otosclerosis is by some regarded as a hyperplasia of bone of an elementary and imperfect type, a form of newgrowth; by others as a degenerative process affecting the organ of hearing as a whole.

According to Berger a positive symptom of mastoiditis which appears frequently, is spasm and rigidity of the upper third of the sterno-mastoid muscle. Both sides should be compared. When associated with a boggy feel around the tip of the mastoid, it is pathognomonic.

Diseases of the nose form one of the most interesting chapters in the book. A strong plea for conservatism in nasal operations is put in by Lewis. This is very timely. Intranasal operations are frequently too extensive. This is especially so with regard to the turbinates.

The tonsils come in for a good deal of space, as befits this important subject. Diathermy, however, receives little mention.

Those who have written on the radium treatment of intrinsic carcinoma of the larynx, are somewhat pessimistic. Orton states that he has seen no good come from radium in carcinoma of the larynx. Progressive hoarseness is the chief danger signal in this disease. It is to be hoped that the pessimists will be proved wrong and that radium will make the place for itself here that it has made in cancer of the tongue and of the breast.

Altogether this is an excellent book and one that can be recommended.

<sup>1</sup> "The Practical Medicine Series: The Eye, Ear, Nose and Throat," Edited by C. P. Small, M.D., A. H. Andrews, M.D., and G. E. Shambaugh, M.D.; Series 1929. Chicago: The Year Book Publishers. Crown 8vo., pp. 574, with illustrations. Price: \$2.50 net.

## The Medical Journal of Australia

SATURDAY, APRIL 19, 1930.

### Post-Graduate Teaching.

It should be unnecessary to draw attention to the value of post-graduate study. All medical practitioners know that, unless they make some effort to keep abreast of progress in medical knowledge, they will be left in the backwash. Practitioners who profess special knowledge in the several branches of medicine, need less stimulation to study than general practitioners. Putting the matter on the lowest plane, that of personal profit, they would soon find, as a result of neglect, that their brother specialists would obtain better results and larger practices than they. The general practitioner may find it easy to persuade himself after a long day's work and with the possibility of a disturbed night's rest, that he is too tired to read one or more of his journals or of the books which an importunate traveller has prevailed on him to buy, or which he has ordered in a moment of good intent. And he may without much difficulty bring himself to believe that whenever he has the opportunity of leaving his practice, it is better to go fishing or shooting than to attend a post-graduate course. It is so easy to drift. The fact to be remembered is that failure to gain a proper understanding of the nature of disease exposes the lives of patients to the risks attendant on unsuitable treatment.

Medical practitioners in Australia have abundant opportunities for improving their knowledge. The written word they may have at all times. All members of the British Medical Association in Australia are supplied with *The British Medical Journal* and *THE MEDICAL JOURNAL OF AUSTRALIA*, journals which are intended primarily for the general practitioner. Of specialist journals there is an enormous number and books are plentiful and relatively cheap. The spoken word and the practical demonstration are available at scientific meetings and at courses of post-graduate instruction. As has been stated

on previous occasions in these pages, the written word, though of undoubted importance, is difficult of use as a systematic means of bringing knowledge up to date. The same may be said of scientific meetings and discussions, though the participants have the benefit of personal communication. Post-graduate courses as arranged by the committees of the several States, have the advantage of being planned with care, so that the student is taken step by step over the essential parts of a certain range of subjects. Courses are of a general or special nature. The Melbourne Permanent Committee for Post-Graduate Work arranges an annual refresher course on lines suitable for the general practitioner. There is an annual course in obstetrics and special courses have been held for those preparing for a higher surgical degree. At the present time a course in pathology is in progress. In New South Wales the Post-Graduate Work Committee of the New South Wales Branch of the British Medical Association, recently created, is pursuing an energetic policy. This committee consists of *ex officio* members, the President, the President-Elect, the Honorary Secretary, the Medical Secretary, the Honorary Treasurer and the Honorary Secretary of the Science and Organization Committee, with Dr. V. M. Coppleson, Dr. Wilfred Evans, Dr. E. H. M. Stephen and Dr. A. S. Walker. A general course arranged by the Branch has been held every year and a special course in obstetrics last year was most successful. In Adelaide the Adelaide Permanent Post-Graduate Committee, constituted on somewhat similar lines to those of the Melbourne committee, has announced its first general course. In Queensland the Queensland Branch of the British Medical Association holds an annual course and in Tasmania post-graduate lectures and demonstrations are held from time to time. More recently there has been a demand, a reasonable and just demand, for the institution of continuous post-graduate teaching. A forward step in this direction will shortly be made. Arrangements have practically been completed for the institution of open demonstrations to be held at 3.30 o'clock p.m. once a week at the teaching hospitals of Sydney. These demonstrations will be available to all medical practitioners. The

committee is to be congratulated on this forward move. It will be successful if an attempt is made to secure some systematic arrangement of teaching, compatible, of course, with the nature of the so-called "clinical material" that is available, and if demonstrators are chosen for their teaching ability and keenness and not according to seniority—one of the bars to efficiency in Australian teaching hospitals. Medical practitioners are earnestly besought to make the fullest possible use of all these facilities. Practical appreciation will result in their extension.

While this appeal is made to medical practitioners, the attention of post-graduate committees may be drawn towards the possibility of cooperation in at any rate one direction. At a later date it may appear advisable to consider cooperation to prevent overlapping in general refresher courses, so that more intensive study may be given to one set of subjects in one centre. The matter for consideration at present has to do with the visits of overseas lecturers. The Melbourne Permanent Committee for Post-Graduate Work has in the past arranged for the visit of lecturers of renown from overseas. By the courtesy of this committee it has sometimes been possible for the lecturers to visit other centres. It should be possible to make some arrangement, satisfactory to all post-graduate committees, by which visits of this kind could be made oftener and of wider radius.

### Current Comment.

#### "AVERTIN."

THE papers by A. Bolliger and Kempson Maddox and by Ellen A. Balaam, published in this issue, are interesting contributions to an important subject. They should be carefully studied by all who are interested in the subject of anaesthesia. The paper by Bolliger and Maddox is of importance not only to laboratory investigators, but also to anaesthetists and surgeons. Their biochemical investigations lie at the root of the matter and their findings in regard to the action of "Avertin" in the presence of nephritis call for particular notice. Balaam has touched only the clinical side. Her histories of sixteen administrations of "Avertin" are the first to be recorded in Australia. The series is admittedly too small to allow of the formation of any general conclusions. She does, however, give

an excellent description of the technique of administration and she demonstrates the clinical advantages, particularly from the point of view of the patient. In the course of her article she refers to a discussion held by the Section of Anaesthetics of the Royal Society of Medicine in November, 1929. It will be useful to give a short account of that discussion in order to attempt the evaluation of the method.<sup>1</sup>

The discussion was opened by J. Blomfield who said that fairly definite limits of dosage were stated, but that even within those limits there may be unusual occurrences. According to Professor Eichholtz even with the "safe" dose of 0.1 gramme per kilogram of body weight there may be dangerous symptoms in weakly people; in persons of normal health he has neither seen nor heard of dangerous symptoms being produced by this dose. Blomfield refers to the death of an apparently normal man after a "safe" dose; this apparently was not his own patient. A big and difficult patient of his received a dose of 0.12 gramme per kilogram prior to the resection of a tumour of the thyroid. This man died twelve hours after operation because he was not able to eliminate his "Avertin." Blomfield describes the induction as extraordinarily satisfactory. In only one-fourth of his cases was a satisfactory anaesthesia obtained with "Avertin" alone. As he gives no indication of what his total is, this statement is worthless as far as general conclusions are concerned. In his opinion the production of a satisfactory anaesthesia depends on the nature of the individual and the character of the operation. His general impression is that "Avertin" is a very useful addition to the available drugs, but that no attempt should be made to use it as a routine in a hospital.

Sir Francis Shipway spoke in the light of 106 administrations. Of the 106 patients 66 were males whose ages ranged from 12 to 72; of the 40 females the ages ranged from 15 to 66. The majority received morphine and scopolamine before they were given "Avertin." He states that the estimation of the correct dose is extremely difficult if full narcosis or even the minimum amount of additional anaesthetic is aimed at; body weight is an unscientific and therefore uncertain guide, because habits, occupation and temperament should be taken into account and these are incalculable. In the alcoholic, the active and the highly strung maximum doses will be necessary and the risk of overdosage will be run. He thinks it better to follow the doses laid down by Eichholtz (0.08 to 0.1 gramme per kilogram) and to be content to aim at a safe, quiet, pleasant induction and to look upon "Avertin" solely as a basal anaesthetic. In 20 of his administrations "Avertin" was used alone; in 31 gas and oxygen were used in addition and this combination seemed to be ideal; in ten ether was added to the gas and oxygen; in three a mixture of chloroform

<sup>1</sup> *Proceedings of the Royal Society of Medicine*, December, 1929.

and ether was given; in one chloroform was given and in 41 ether was used. Shipway also refers to a recommendation made by Professor Eichholtz that attention should be paid to the rapidity of the onset of sleep or rapid deepening of sleep; if this should occur, the remainder of the injection should be at once let out of the bowel. He adds that this precaution can only be adopted in clinics where the injection is either given by the same person who can make herself familiar with the phenomena of what may be termed a normal induction, or supervised by an anaesthetist who is fully acquainted with the varying reactions of patients to anaesthetics. It would appear from this that Shipway is prepared to allow the injection to be given and the patient to be under the supervision of a nurse or other person who is not a medical practitioner. This is a most objectionable practice. That it possibly obtains in other countries, matters not. The patient's life is in the hands of the person giving the injection and superintending its action. This person should be a medical practitioner "fully acquainted with the varying reactions of patients to anaesthetics" and it may be added, prepared both by experience and with apparatus to act in the event of any untoward occurrence.

James Young said that he had used "Avertin" for 154 unselected patients in his hospital and private gynaecological practice. In this series there were two deaths, one after hysterectomy for uterine prolapse and the other in a case of long standing pelvic infection. In neither instance could the death be attributed to the "Avertin."

H. E. G. Boyle drew attention to the fact that most of the patients reported at the discussion had received heavy doses of morphine or morphine and scopolamine beforehand. This must place patients in a somewhat dangerous position. If "Avertin" sent people to sleep so easily, why could not a smaller quantity be given than that mentioned by Blomfield and Shipway, so that patients would be merely asleep. The "Avertin" could then be used, not as an anaesthetic, but as a form of premedication before an anaesthetic was given.

Ramsey Phillips referred to the beneficial action of carbon dioxide in the treatment of anoxaemia occurring during "Avertin" narcosis.

Geoffrey Keynes said that he intended to use "Avertin" in the treatment of patients with exophthalmic goitre prior to the use of local anaesthesia. These patients are always apprehensive and all operations are a severe ordeal for them. This suggestion is a most reasonable one and should not be forgotten.

In drawing any conclusions from this discussion it must be remembered that most extensive experiments have been carried out in Germany on this drug. The extraordinary precautions adopted before the drug was put on to the market and even before supplies were made available to competent observers must be commended. This will probably prevent the unwise use of the drug by unskilled persons so that

it will not fall into disrepute as so many new means of treatment have fallen from over-enthusiasm or foolishness. The first thing to be remembered is that with full doses there is not a large margin of safety. If, then, the choice lies between "Avertin" in full doses and another form of anaesthesia, the latter must be used. With a patient who is particularly apprehensive either of induction of anaesthesia or of the post-anaesthetic symptoms, or in whom it is desirable from the surgical point of view that post-anaesthetic symptoms should not occur, full doses may perhaps be given. As a rule, even in these circumstances, additional anaesthetics, such as gas and oxygen or ether, will be required as well. It will be wisest at the present time to follow Boyle's suggestion and to regard "Avertin" as suitable for premedication. It is much better to widen the indications for its use in the light of experience than to cut them down in the shadow of disaster.

#### LEUCOCYTOSIS IN SCARLET FEVER.

In many clinical conditions examination of the leucocytes yields information which is valuable from the point of view of prognosis. It has been claimed that when patients with scarlet fever are treated by antistreptococcal serum, non-septic complications are less likely to occur, but that there is no influence on those of a septic nature. Margaret E. Wylie has investigated the question of leucocytosis in scarlet fever.<sup>1</sup> She has not concerned herself with eosinophilia, because this has already been fully investigated. It has been discussed in these pages. The patients investigated by her numbered forty-four. Ten were moderately ill (Group I), twenty-seven were acutely ill (Group II), two were very acutely ill (Group III), four had toxic scarlet fever (Group IV) and one had septic scarlet fever (Group V). The number of patients is too small to justify the formation of definite general conclusions, but Wylie's observations are none the less interesting. The blood of the patients was examined on the day of admission and on the third and seventh day thereafter. The initial leucocytosis in the five groups is tabulated and it is clear from the average figures that the leucocyte count is a less reliable index of the severity of the disease than the general clinical picture. The patients in Group III had a definitely higher leucocytosis; there were only two of them, however, and they required a large dose of serum. The criteria as to the requirement of serum are not stated; the patients in Group IV and Group V required less serum than those in Group III. It was noted that in both complicated and uncomplicated cases there was a pronounced fall in the white cell count between the first and the third days. The administration of antitoxin had no influence on the leucocyte count. The constant lymphocytosis was not related to the presence of complications or the giving of serum.

<sup>1</sup> *The Journal of Infectious Diseases*, November, 1929.

## Abstracts from Current Medical Literature.

### OPHTHALMOLOGY.

#### The Newer Physiology of the Eye.

W. S. DUKE-ELDER (*The Lancet*, January 4, 1930) invites his readers to look at the eye as an infinitude of molecules and atoms, each travelling in its own appointed path controlled by complex and unalterable forces. These molecules are partitioned off by membranes through which in certain circumstances they may pass. Each molecule of salt in solution is broken up into two ions, each of which carries an electric charge, one positive and the other negative. Free diffusion of all ions equally is precluded by the semipermeability of the membranes and this unequal concentration on the two sides of the membrane at once involves the development of hydrostatic, osmotic and electrostatic forces. When these forces are made to balance, there is a state of thermodynamical equilibrium. This equilibrium, as far as the eye is concerned, may be considered under four headings, namely: (i) The equilibrium between the blood plasma in the capillaries and the intraocular fluid; (ii) that between the intraocular fluid and the vitreous body; (iii) that between the intraocular fluid and the lens; (iv) that between the blood plasma in the chorio-capillaries and the sensory epithelium of the retina, if it be assumed for the sake of simplicity that the blood possesses two kinds of molecules only—large molecules (protein, such as sodium albuminate), the colloid part of which cannot get through the membrane, and smaller molecules which can. Some of the latter are broken up into particles which are ionized and carry an electric charge (salt), and some, being non-electrolytes, are not thus broken up (sugar). Across the membrane the negatively charged albuminate is held back and with it for electrostatic reasons some of the positively charged sodium ions will be retained also. Donnan has shown that the products of their concentrations are equal on both sides of the membrane. These theoretical considerations are remarkably attained in the actual analysis of the aqueous humour in comparison with that of the blood plasma. The vitreous has been shown to be a simple and homogeneous jelly or gel; the fibrillar appearances seen histologically being artifacts and the membranous appearances seen by the slit-lamp similarly optical artifacts. It is an elastic and turgescible gel, capable of swelling and shrinking; it tends to swell if the concentration of hydrogen ions is increased, and to shrink if this concentration becomes smaller. If its metabolism is upset, the whole gel structure breaks down and turns fluid, the residual protein material being thrown out as the vitreous opacities seen clinically. The osmotic pressure of the lens is higher than that of the aqueous which sur-

rounds it. Owing to the tonic pull of the capsule through the zonula, the internal tension of the lens is kept at a higher level than the remaining tissues of the eye and therefore it follows that the osmotic tendency of a fluid to enter the lens is counterbalanced by the opposing force exercised by the tension of the capsule favouring the hydrostatic diffusion of fluid out of the lens. The effects of the disruption of these forces are seen in their most dramatic form when rupture of the capsule is followed by traumatic cataract and also when the osmotic balance is disorganized in diabetes resulting, if the process is mild, in diabetic cataract. The sensory epithelium of the retina receives its nourishment by dialization through the chorio-capillaries. Experimental evidence has shown that upset of this process produces a derangement of the physico-chemical activity of the percipient elements of the retina; such is apparent clinically as a scotoma. There are probably two main factors in the aetiology of glaucoma which perhaps determine two types of the disease. The first is a derangement of the capillaries involving a dilatation, an increased permeability with abundant exudation of fibrinous coagulum. The second is a swelling of the vitreous body causing compression and flattening of the uveal tract and all the tissues of the eye. Idiopathic detachment of the retina probably results from changes of the opposite kind, namely, a shrinkage and liquefaction of the vitreous gel.

#### Lipæmia Retinalis in a Diabetic.

C. E. G. SHANNON AND H. K. MOHLER (*American Journal of Ophthalmology*, December, 1929) relate the history of a man of forty-two admitted to hospital in a drowsy condition. Seven years previously he had started treatment for diabetes. At the time of admission there was a percentage of 3.3 of sugar in the urine and traces of acetone and diacetic acid were present. A specimen of blood separated into an upper half of a creamy colour and a lower dark brown half. Examination of the fundi revealed a typical picture of *lipæmia retinalis*. The disc was greyish or waxy in colour and the vessels broad and ribbon-like, of a distinct salmon-like colour. The arteries and veins were indistinguishable. Five days after "Insulin" treatment they had returned to normal. Only thirty-five cases of *lipæmia retinalis* have been reported. The disturbance of metabolism in diabetes is more evident as regards the carbohydrates, but it is known that the fat of the body is handled abnormally in diabetes and is present in excess in the blood stream and the liver.

#### Parathyroid Tetany and Cataract.

L. COLE's patient (*The Lancet*, January 4, 1930) was a woman of thirty-four who a year previously had had both lateral lobes of her thyroid completely removed and the middle lobe left. Within a week she noticed stiffness of her fingers, tingling of her hands and cramp in her tongue.

Later on she began to have fits and her sight failed. On examination she was found to have cataract in both eyes. Chvostek's sign was elicited. Light percussion over the branches of the facial nerve below the ear caused twitching of the corners of the mouth. Analysis of thirty-eight recorded cases shows that the results of partial or complete removal of the parathyroid glands consist in (i) alterations of the calcium content of the serum with tetany, (ii) changes in the lenses, nails, teeth and hair. It is important in removing the thyroid to leave the upper posterior part of at least one lobe. In the present patient treatment with parathormone had no effect on the cataracts. A high calcium diet, 1,200 cubic centimetres (two pints) of milk and two eggs and 48 grammes (twelve drachms) of calcium lactate daily, keep the serum calcium between five and eight milligrammes and the tetany latent.

#### Dendritic Keratitis Following Therapeutic Inoculation of Malaria.

W. C. FINNOFF (*American Journal of Ophthalmology*, December, 1929) reports the history of a man, aged thirty-seven, complaining of parietic symptoms and giving a history of a positive Wassermann reaction. A diagnosis of neurosyphilis was made and he was inoculated with tertian malaria. After ten days he began to have the chill and fever attacks at regular intervals and after the fourth attack felt pain in the left eye which soon presented a typical herpetic infiltrate of the cornea. Antimalarial treatment was instituted and the ulcer slowly healed with considerable loss of sight. A second patient, aged forty-two years, was inoculated with malaria for syphilitic paresis. After a week he began to have daily bouts of fever for ten days when the malarial symptoms ceased. Three days later he developed dendritic keratitis. For many years the relationship between malaria and dendritic keratitis has been discussed. A patient treated in this manner should be warned of possible danger to the eye.

#### Food Poisoning in Relation to Ophthalmology.

C. H. SWAT (*American Journal of Ophthalmology*, December, 1929) has carried out a series of experiments on dogs, rabbits and other animals by injecting the toxins of the *Bacillus botulinus* and observing the changes produced in the nervous system and in the eye. Van Ermengem in 1897 described the botulinus syndrome as a collection of neuromuscular symptoms including external and internal ophthalmoplegia with diplopia and internal strabismus. The three types of botulinus toxin, known as A, B and C, were employed. All the animals exhibited dysphagia and in many instances dryness of the cornea, episcleritis and paralyses of the limbs and neck. The toxin of the *Clostridium botulinum* is the only one that causes eye symptoms. In the nuclei of the third and fourth cranial nerves many changes were observed,

such as round cell infiltration, distension of capillaries with erythrocytes and complete disintegration of the ganglion cells. Similar changes were noted in other parts of the mid-brain. In the retina were seen fat formation and vacuolization of the ganglion cells. The changes involved also the pigmented cells and the chorioid and ciliary bodies.

## OTOLOGY AND LARYNGOLOGY.

### The Surgical Anatomy of the Tonsil and Tonsillectomy.

R. SCOTT STEVENSON (*The Practitioner*, January, 1930) describes the lymphoid tissue surrounding the entrance to the respiratory and alimentary passages and points out the importance of the muscular attachment of the tonsil in the operation of tonsil dissection. He states that all the lymphoid tissue in Waldeyer's ring is liable to infection and enlargement, but those parts of it in which crypts are insignificant, have little or no importance in relation to systemic infection. The crypts are large and extend deeply into the tissue of the tonsil. In the lingual tonsil the crypts are not deep, but in the pharyngeal tonsil (adenoids) there are extensive and complicated infoldings. The faucial tonsil is not a lymph gland covered with a capsule, but consists of a mass of lymphoid tissue embedded in a triangular fossa, formed between the glosso-palatine and the pharyngo-palatine pillars of the fauces and the side of the tongue. The deep surface of the tonsil is separated from its muscular bed by some loose areolar tissue. When the tonsil is removed, the so-called capsule seen covering it after operation is in reality a layer of this connective tissue which forms part of the sheath of the muscles of the tonsillar bed. He points out that careful dissection shows that the superior constrictor is in relation in its inner surface with the *palato-pharyngeus* muscle and the pharyngeal aponeurosis and that the superior constrictor is separated from the tonsil by the *palato-pharyngeus*. Part of the *palato-pharyngeus* muscle forms the posterior pillar of the fauces and defines the bed of the tonsil behind. In front it merges with the buccopharyngeal fascia. Certain fibres of the *palato-pharyngeus* are attached to the deep surface of the tonsil and on dissection are found actually embedded in the substance of the tonsil, so that it is impossible to remove the tonsil without removing portion of the muscle fibres also. If the muscular fibres are abundant and there is a definite infratonsillar lobe, the employment of a snare to complete the enucleation must eventually leave a large piece of lymphoid tissue behind. The same holds good with regard to the employment of the guillotine, even in children. To remove a tonsil completely in 100% of cases he recommends the method of slow blunt dissection. The muscular attachment of the *palato-pharyngeus* to the tonsil is gently teased through. The dissection

must be continued onwards, following the line of aponeurotic cleavage until the whole of the lymphoid mass together with its infratonsillar portion is removed; it may be necessary to extend the dissection well down into the pharynx. The author is of the opinion that it is unnecessary to remove any part of the lingual tonsil and concludes that in the complete operation there is no place for the snare or the guillotine.

### Radium Treatment of Intrinsic Carcinoma of the Larynx.

DOUGLAS HARMER AND N. S. FINZI (*The Practitioner*, January, 1930) describe a method whereby radium needles are placed outside and not into an intrinsic carcinoma of the larynx. A skin incision is made over the thyroid cartilage on the affected side, starting at the centre of the hyoid bone and extending outwards and downwards along the posterior border of the thyroid cartilage. On the other hand a "collar" incision may be made transversely across the middle of the thyroid cartilage. The latter is perhaps preferable, especially if both sides of the larynx require treatment. The infrahyoid muscles are exposed and split longitudinally. The lateral aspect of the thyroid cartilage is exposed, the perichondrium divided and stripped backwards and forwards. The greater part of the cartilage is then resected, leaving a large window and a framework of four margins. The outer surface of the growth covered by perichondrium is thus exposed. It is important not to destroy this capsule or to cut into the growth. The cartilage is removed for two reasons: to allow the needles to be placed as close to the growth as possible and to prevent the perichondritis or necrosis which may be caused by the radium. From five to ten radium needles are then inserted; they are placed parallel to one another and vertical. To keep them in position the ends of the needles are tucked under the framework of the cartilage. Care is taken that the needles do not penetrate the growth or the larynx. If the growth is subglottic, the needles are pushed inside the cricoid ring, great care being taken to avoid perforating the air passage. To obtain uniform irradiation the active part of the needles must extend well beyond the limits of the growth. Only the central part of a needle contains radium and about six millimetres at each end are inactive. Each needle has attached to it a piece of linen thread soaked in a one in a thousand solution of flavine. The threads are all tied together and buried beneath the muscles. Double sutures are inserted into the skin, half of them being tied at once to close the wound completely and the other half left so that they can be tied later after the radium has been removed. No drainage is employed and the skin incision is completely sealed with a collodion dressing. If the growth has extended across the middle line, a second window is made in the thyroid cartilage on the opposite side and

needles are buried there also. When necessary, a low tracheotomy is then performed. Details of dosage are given.

### The Chorda Tympani Nerve in Otology.

M. VLASTO (*The Journal of Laryngology and Otology*, January, 1930), on investigating the effect on the *chorda tympani* nerve of injury and disease of the middle ear, found that observations on the sense of taste are tedious and frequently unreliable. He tested the taste with maximal stimuli and with the elimination as far as possible of unreliable witnesses. Aqueous solutions of salt, sugar and quinine sulphate were used. One of the factors which made observations tedious and difficult to interpret, was the variation in the threshold of sense of taste of normal subjects. Certain facts can be laid down as proved: First, that a considerable number of patients with middle ear suppuration have a lesion of the *chorda tympani*; secondly, that the *chorda tympani* is most frequently the site of a lesion where the middle ear disease is of long standing, affects the attic and is attended by cholesteatoma; thirdly, that in many advanced cases of middle ear disease the integrity of the *chorda tympani* is completely preserved. No useful deduction as to extent of the disease can therefore be drawn from the integrity or destruction of the *chorda tympani* nerve. The author endeavoured to obtain objective evidence. The object of the inquiry was to ascertain whether or not changes occurred in the submaxillary gland as a result of interference with the continuity of the *chorda tympani* in the tympanic cavity. The first patient had a history of otorrhoea of fifteen years' duration and extensive attic disease on the left side. The right ear was normal. Taste testing gave the following result. With the right ear the result was positive for sweet, salt and bitter. With the left ear there was no reaction for sweet and bitter and possibly a slight reaction for salt. The patient died from intracranial complications ten days after the above tests were made. Sections were made of both submaxillary glands. The right gland sections were those of an ordinary normal gland, the weight of the gland being 7.94 grammes. The left gland section revealed definite changes of an inflammatory and degenerative character, the weight of the gland being 6.91 grammes. The second patient had had a radical mastoid operation performed on the right ear seven years before. On examination of sections of both submaxillary glands under high power there was found to be a distinct difference on the two sides. It is undecided whether the change in the right gland was pathological (liquefactive degeneration) or some purely physiological change. The author submits that the *chorda tympani* may be the site of a lesion in suppurative disease of the tympanic cavity and that the nerve is always destroyed by the radical mastoid operation with permanent effect.

## British Medical Association News.

### SCIENTIFIC.

A MEETING OF THE QUEENSLAND BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held at the Geology Lecture Theatre, University of Queensland, on February 7, 1930, Dr. S. F. McDONALD, the President in the chair.

#### William Harvey and the Circulation of the Blood.

A cinema film was shown, entitled: "William Harvey and the Circulation of the Blood." Before the showing of the film Dr. S. F. McDonald read a paper entitled "Harvey" (see page 508).

The film opened with Cornelius Jansen's portrait of Harvey, which hangs in the Royal College of Physicians, London. The famous physician was seated. The hands of the picture were seen on an enlarged scale and were represented as moving to take up an ancient treatise. Over his shoulder could be seen a few pages of Galen's "*De Venarum et Arteriarum Sectione*" and his "*De Usu Partium*," of the "*De Fabrica*" of Vesalius and the "*Questiones Peripateticæ*" of Cæsalpinus, these being among the relevant works to which Harvey had access. Galen's doctrines, the dominant views in Harvey's time, were summed up briefly by means of a diagram. They were the doctrines that had formed Harvey's starting point. In part he had substantiated Galen's views, in large part he had refuted them as a result of the experiments which the film exemplified, presenting them in five sections, each marked by an appropriate heading and diagram.

In the first section, that dealing with auricular injection, evidence was presented against the view that the ventricle fills by suction. It was the evidence of the normal sequence of chamber contraction and of the pumping of blood from auricle to ventricle.

In the second section, that of ventricular injection, were the main heads of evidence that the arteries are passive, that they are filled by the forcible ejection of blood from the ventricle into them. When the ventricle contracted it paled, became small and hard, the arteries expanded and from the cut arteries blood gushed forth. A brief summary of previous views relating to the pulmonary circulation was interposed, and the film proceeded to Harvey's third series of demonstrations.

In the third section, that of passage through the lungs, pores in the interventricular septum could not be demonstrated. The blood was shown to leave the right heart by the pulmonary artery; it could not return past the pulmonary valves. The presence of a way through the lungs to the left heart was demonstrated by injections. In three steps Harvey had shown that blood passes from the veins to the arteries, following a pulmonary course in so doing.

He now passed on to his most crucial observations and original conclusions, illustrated in sections four and five. It was at this stage that he first expressed the view of continuous motion and of movement in a circle; here his views diverged most notably from those of his predecessors.

In section four, in stating the evidence of continuous movement from veins to arteries he laid stress upon the quantity of blood which he calculated must be ejected from the left ventricle at each systole; this blood did not return. He calculated from simple data that the heart must within a short space of time eject more blood than was to be found in the whole body. Continuous motion could be displayed by obstructing the main veins or main artery, for the vessel emptied beyond the obstruction and the blood accumulated behind it in each case.

The passage from arteries to veins formed the fifth section. The movements of blood in the human limb were studied; by obstructing now the artery and now the veins, the former was shown to fill from the centre, the latter from the periphery. Similar conclusions were formed by noting the effects of cutting through veins and arteries of living animals in their length; the former bled peripherally, the

latter centrally. Finally, the function of the venous valves, their control of the direction of the venous blood stream was fully displayed in the human limb.

His experiments complete, Harvey wrote his book. The last part of the film represented him turning the pages of this work; his hands closed the book and laid it on one side, before becoming still.

### NOMINATIONS AND ELECTIONS.

THE UNDERMENTIONED have been nominated for election as members of the New South Wales Branch of the British Medical Association:

Lane, Albert Stephen, M.B., 1923 (Univ. Sydney), Camooweal, Queensland.  
Jones, Reginald Stuart, M.B., Ch.M., 1926 (Univ. Sydney), F.R.C.S., 1929 (Univ. Edinburgh), 10, William Street, Double Bay.

## Medical Societies.

### THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA.

A MEETING OF THE MEDICAL SCIENCES CLUB OF SOUTH AUSTRALIA was held at the University of Adelaide, on August 2, 1929.

#### The Anæsthetic Action of Magnesium Sulphate.

MR. M. L. MITCHELL gave an account of some work on magnesium sulphate anæsthesia done by himself in conjunction with Dr. Hübbe and Dr. Hicks. This had been the outcome of some observations made in the pharmacology class and it had been noted by Professor Hicks that the concentrations of magnesium sulphate necessary to produce full anæsthesia were vastly in excess of those used by Gwathmey in his morphine magnesium sulphate anæsthesia in obstetrics.

Gwathmey claimed that there was a synergic action between morphine and magnesium sulphate. It did not appear that the quantities of magnesium sulphate used, even if synergism were claimed, could possibly have any effect upon the anæsthesia. In order to test this rabbits had been injected intramuscularly with a sterile 25% solution of magnesium sulphate with doses varying from two to three cubic centimetres per kilogram of body weight. The progress of the anæsthesia had been closely watched and the times of disappearance of various reflexes recorded. At the same time the animals had been bled and the blood analysed for magnesium as well as the calcium content. It had been found that the symptoms of depressant action began when the serum magnesium reached eight milligrammes *per centum*, while profound narcosis was associated with twenty milligrammes or more of magnesium *per hundred centigrammes*.

In obstetrical analgesia when two or three intramuscular injections of two cubic centimetres of 50% magnesium sulphate solution were administered, the serum magnesium could not reach more than three milligrammes *per centum* and would probably be even less. It did not therefore appear that the presence of the magnesium could have a very profound influence.

An interesting point arising out of the same investigation was the relation of the calcium to the magnesium. The calcium in the present series of cases showed little variation and although the work was at present in being, it would appear that the effect of the magnesium was not due to the withdrawal of calcium from the tissues, but to the direct effect of the magnesium. The antidote effect of the soluble calcium would be on this conception merely an antagonising effect. This point, however, could be decided only when the question of diffusible and non-diffusible calcium was investigated in this connexion.

DR. L. V. BULL cited cases of oxalic poisoning of sheep, previously reported. He had been unable to use the blood calcium as an index of the degree of poisoning. He quoted a reference citing the cerebro-spinal fluid as a source of diffusible calcium, and asked if the effect was due to the ratio of calcium and potassium to magnesium and sodium respectively.

Mr. Mitchell said that he thought the ratio would be better expressed as calcium and magnesium to potassium and sodium.

Dr. Bull referred to feeding experiments in which calcium-rich and magnesium-rich diets had been used and in which they had had no effect upon bone calcium *et cetera*.

Mr. Mitchell said that the nature of the salt used would be very important.

PROFESSOR J. A. PRESCOTT drew attention to the rapidity of recovery of the animals when calcium was administered as compared with the rate of onset of narcosis.

PROFESSOR C. S. HICKS again raised the question of non-diffusible calcium which might be slowly displaced by the magnesium and rapidly replaced by injection of soluble calcium.

#### Carbon Dioxide and the Blood.

Professor Hicks then dealt with some points arising out of the paper of Dr. Ray Hone read at the previous meeting. He pointed out that the place of the plasma protein in the transference of carbon dioxide had in the past been considered of major importance, but that since the work of Haldane and Christiansen attention had been directed to the part played by hæmoglobin in that connexion. Under the circumstances it would appear that the corpuscles were responsible for the supply of 80% to 85% of available base, this availability being brought about by the change from oxyhæmoglobin to hæmoglobin, while in addition the Hamburger phenomenon, originally foreshadowed by Zuntz's observations in 1867, was responsible for the carriage of a further 10%, the remaining carriage of carbon dioxide being therefore left to the protein in its change from sodium proteinate to protein and to the phosphates.

It was stated by some authors that the protein was responsible for some 25% of the carriage of carbon dioxide and the latest edition of Professor Robertson's "Principles of Biochemistry" placed the amount of carbon dioxide carried by the function of the corpuscles, as not less than 75%, leaving the remainder to be carried by the subsidiary methods of carbon dioxide carriage, namely, the proteins and other accessory factors.

A second point dealt with was the query by Dr. Hone that sufficient unaltered protein could reach the blood in order to appear in the urine unchanged. The literature on the subject went back a long way and unfortunately the journals were not available, but it was a well established fact that egg albumin, provided it was taken in sufficient quantity—that is to say as many as fourteen to fifteen eggs—would in most people produce an albuminuria; while a smaller quantity would do the same in some more sensitive individuals. The first papers had appeared in 1864 and a great deal of work had been done upon the subject between 1864 and 1904. It had been found by Eichorst in 1871 that egg albumin was rendered absorbable by the intestinal epithelium upon the addition of sodium chloride and Voit and Bauer (1869) stated that it was utilized in that state. Luciani (1913) had reviewed the literature and had stated that the reason for the action of sodium chloride was not known, but that the effects had been positively confirmed and established.

Landois had shown that after the ingestion of twenty to forty eggs with sodium chloride albuminuria appeared in from four to ten hours the albumin content of the urine increasing until the third day and disappearing at the end of five days. Adami, Posner and Ribbert had shown that the proteins directly through the capsule gained the Malpighian tubes. The albuminuria produced in this way was not in the least to be confused with the albuminuria to be found in athletes after severe exertion. The same phenomenon was produced more readily by the intravenous injection of albumin.

It had been shown that more albumin was passed within the twenty-four hours than the total injected and Ascoli in 1902 had shown by antigen methods that most of the protein was egg albumin, the excess over the total ingested being blood protein. Ascoli and Oppenheimer had succeeded in sensitizing animals by feeding them with large amounts of ovalbumin and they had demonstrated by precipitin reactions the presence of the egg albumin in both the blood and the urine of these animals. Lesné and Dreyfus had cleared up many contradictory conclusions when attempts to repeat this work were made, by showing that sensitization could be obtained in all cases if the albumin was directly introduced into the large intestine. Besredka had been able to desensitize previously sensitized animals by the rectal injection of the sensitizing protein (egg white).

Whatever was the cause of the access of the unaltered protein to the blood, the fact remained; and some very interesting and remarkable work on this subject had been carried out by Andrews and his coworkers in the previous three years. These workers had succeeded in following the phenomena very closely by an application of a highly sensitive precipitin reaction and they had concluded that the first effect of the protein on reaching the blood was to produce damage to the liver in such a way as to set free liver protein in the circulating blood. These proteins together with the foreign proteins appeared in the urine and were followed secondarily by the serum protein.

The interesting feature, however, was the new light which it threw upon certain forms of nephritis, because it was found by these workers that the first protein to appear in the urine in nephritis was liver protein, the tests for the same being sensitive to one part in a million. Only after the passage of the liver protein did the kidney capsule become damaged and pass the serum protein. The kidney in such cases was thus only only secondarily involved.

These same workers had shown that the urinary protein in the nephritic cases cited contained a highly dispersed form of serum protein, causing the same precipitin reactions as serum protein, but differing in that it was diffusible through a collodion membrane. This protein was highly toxic, fifty milligrammes given intravenously causing death after typical nephritic coma in twenty-four to forty-eight hours. Further, serum from uræmic patients produced the same effect and from such serum a similar highly dispersed blood protein could be prepared.

These workers had also shown that the full symptoms of uræmia could be produced by lowering the pH value of the blood of an animal deprived of its "free" water, such an animal being quite normal until the change of hydrogen ion concentration, when it died rapidly. In other words, the uræmic symptoms would appear to be due to osmotic effects depending on the imbibition power to the tissue colloids. It was a matter of clinical knowledge that uræmia was very often unassociated with nitrogen retention.

#### THE BRISBANE HOSPITAL CLINICAL SOCIETY.

A MEETING OF THE BRISBANE HOSPITAL CLINICAL SOCIETY was held at the Brisbane General Hospital on February 13, 1930, DR. EUSTACE RUSSELL in the chair.

#### Adiposis Dolorosa.

DR. JOHN BOSTOCK showed a patient with *adiposis dolorosa*. He pointed out that the condition was characterized by painful fatty tumours, psychic disorders and vegetative symptoms. The causation was stated to be doubtful. Whilst some authorities stressed the thyroid influence, others paid more attention to the pituitary and subthalamic regions. The patient shown illustrated the benefits of thyroid medication and at the same time the presence of well marked hysteria was suggestive of a lesion somewhere in the basal nuclei.

The patient was a single woman, aged thirty-three years, who for years had had painful swelling confined to the left side of the body. They had occurred on the arm, leg

and body. At the time of demonstration an ill-defined, painful mass was present on the posterior part of the neck. She had just recovered from a pronounced hysterical spasm of the left upper extremity. X ray examination revealed no abnormality of the pituitary fossa. The Wassermann test applied to the blood had yielded no reaction.

Treatment consisted in the administration of extract of thyroid 0.3 gramme (five grains) every day and hyoscine hydrobromide 0.43 milligramme (one one hundred and fiftieth of a grain) and tincture of opium 0.6 mil (ten minims) three times a day during the preliminary period when pain and spasm were acute. The patient admitted to improvement.

#### Chronic Nephritis.

Dr. L. J. NYE showed a male patient, aged twenty-seven years, who was suffering from chronic nephritis. He stated that this patient had a history similar to those of many sufferers with chronic nephritis in Queensland. He had spent his childhood in a house on high blocks, the paint of which was dry and powdery. He was the only member of his family who was a nail biter and the only sufferer from nephritis. His physical development was stunted, as was noticed in all the patients with lead poisoning, and he gave no history of any previous illness. Dr. Nye considered that many of these patients with nephritis were suffering from plumbism unrecognized in childhood.

#### Congenital Sigmoid Looping of the Oesophagus.

Dr. Nye's second patient suffered from a congenital sigmoid looping of the oesophagus. The patient, a female, aged sixty, had complained of periodic attacks of epigastric distress and vomiting. Test meal findings had revealed complete achlorhydria with definite evidence of stasis typical of advanced gastric carcinoma, but X ray examination had revealed a definite sacculum of the oesophagus about ten centimetres (four inches) in diameter with no obstruction at the cardia. The Rehfuss tube had apparently not reached the stomach, but had remained in this sac throughout the test. The sac had been washed out and the patient had progressed satisfactorily since.

#### Loose Bodies in the Knee Joint.

Dr. NEVILLE SUTTON showed a half-caste woman of forty-three who gave a history of spraining her right knee ten years previously. The knee had become very swollen, but had gradually subsided and she had had very little trouble for seven years. Latterly the knee had been locking in flexion and sometimes she had been able to manipulate it herself and get it free, but at other times she had had to obtain medical attention. The locking had become more frequent and more persistent the last year and when Dr. Sutton saw her in December, 1929, she had had her knee locked in flexion for a fortnight, the longest period she had suffered it. Dr. Sutton had been able to relieve it by manipulation, but she had not got complete extension by about 10°. The knee had been somewhat swollen generally and there had been definite crepitus on motion. The right thigh had been wasted and considerably smaller than the left. There had been some slight degree of *genu valgum*. A radiogram had revealed osteoarthritic changes with three or more calcified bodies present.

The knee joint had been opened on January 9 by a Timbrell Fisher's incision and four loose bodies had been removed. The infrapatellar pad had been thickened and congested and it had been removed. Two osteophytic outgrowths had been chiselled away from the anterior margin of the articular surface of the femur. The knee had been tightly bandaged and rested on a pillow. There had been no effusion and active motion had been encouraged from the first. She had been allowed out of bed on the twelfth day and had been having massage to the wasted muscles. At the time of the meeting she could flex the knee to 80° and extension lacked about 5°.

This patient presented a history of an original severe sprain with subsequent development of osteoarthritis with loose bodies which appeared to be detached osteophytes,

as they exactly resembled those that were still attached to the femur. The left knee joint was practically normal.

The X ray films and the bodies removed at operation were then demonstrated.

#### Prostatectomy.

Dr. Sutton also showed a man, aged sixty-seven, who had had difficulty in passing urine, gradually increasing for the past ten years. He had been getting up at night about twice. He had had an attack of acute retention about a year previously. He had got retention again on December 20, 1929, and his bladder had been catheterized twice that day and he had come into hospital the next day, when a catheter was tied in. His prostate had been moderately enlarged. His renal function and his general condition had been entirely satisfactory, but he had got a mild attack of epididymitis after being five days in hospital. This, however, had quickly settled down and on January 9 suprapubic prostatectomy with complete closure of the bladder according to the technique of Dr. Harry Harris had been performed. Dr. Sutton then briefly described the operation. The wound had healed and the catheter had been removed on the ninth day. For four or five days after this there had been a small leakage of urine through the pinhole where the silkworm gut retention suture had emerged in the wound. He had passed urine a few hours after the catheter was taken out and had made steady progress, holding his urine for longer periods and losing all pain and soreness. He had been up on the fifteenth day and had been discharged four weeks after the operation.

Dr. Sutton said that his object in showing this patient was twofold. In the first place criticisms had been raised against the technique on the ground that it was a book operation and not practicable; and secondly he considered it was the ideal form of operation and represented a finished form of the previous operation.

Dr. Harry Harris performed the operation with a brilliant perfection of technique and attention to detail that made it a delight to watch him, and although Dr. Sutton could not pretend to any such achievement, nevertheless he showed the patient to prove that this could be learned and emulated by anyone with average surgical skill in these operations and with sufficient enthusiasm; in such hands it was a successful procedure. Harris had a long series of cases; this was the first in which he (Dr. Sutton) had completed the operation and closed the bladder.

In regard to the claims that this represented the ideal and completed operation there had been some difference of opinion and many of its features had been criticized.

As far as the small incision was concerned, it had been asked: "Why cramp yourself for room when you can apparently make large incisions in the bladder with impunity?" Small wounds in the bladder were less likely to leak than large ones and with this technique and the special instruments perfect vision was obtained and actually more exact and purposeful suturing was done at the base of the bladder than had been described in any of the so-called open operations, the actual bleeding points were seen, secured and tied off in the sutures. Post-operative hernia was very much less likely to occur; it was by no means uncommon with ordinary open drainage, as Dr. Sutton had seen in his own patients and in those of other surgeons. The after treatment was easy, clean and very much less irksome to the patient; he went straight ahead and, as they could see, had a small linear scar healed by first intention. Above all the hæmorrhage was definitely arrested on the operating table and not left "in the lap of the gods" or dealt with by pressure of a gauze pad or an inflated bag—poor substitutes for a ligature. Finally, a large raw cavity was closed in and lined with mucous membrane as far as possible and thus scar tissue formation was reduced to a minimum.

Hence Dr. Sutton considered it an ideal procedure, always supposing a clean bladder could be obtained. It was not suitable for old neglected patients who had to have a preliminary suprapubic cystostomy to overcome sepsis and damaged kidney function. Harris prepared very successfully many of his patients with an indwelling catheter without having recourse to suprapubic drainage and the

thesis that all prostatectomy operations should be two-stage operations he considered, like most generalizations in surgery, unsound.

The moral to his mind was that here was another disease in which early operative treatment should be stressed.

#### Carcinoma of the Common Bile Duct.

Dr. J. DUBIG showed a specimen of carcinoma of the common bile duct involving the junction of the cystic and hepatic ducts. The patient had died with jaundice at the age of eighty years.

He had been in Dr. Alex Murphy's ward. The liver had been enlarged and it had been thought that he had a growth pressing on the bile duct, but at *post mortem* examination the carcinoma had been discovered. The enlarged liver resembled that found in biliary cirrhosis.

### Special Correspondence.

#### CANADA LETTER.

By OUR SPECIAL CORRESPONDENT.

##### Radiology.

THE fifteenth annual meeting of the Radiological Society of North America met in Toronto during the first week of December, 1929, in the new palatial hotel of the Canadian Pacific Railway, "The Royal York." It may be mentioned in passing that this hotel is in direct connexion, by an underground passage with the Union Station so that readers of this journal who may pass through Toronto on their way to or from Winnipeg where the British and Canadian Medical Associations meet during the last week of August, 1930, can find without the slightest delay or inconvenience accommodation in a new and luxuriously equipped hotel.

The programme for this meeting provided papers and discussions that can probably be most tersely expressed as the "best tips" in Röntgenology and radiology. The whole field in these branches was fully covered and a very valuable contribution made to the science and art of medicine. The papers and discussions in the cancer symposium went very exhaustively into the cancer problem and very strongly stressed that the great value of X rays and radium in the early stages of this disease. The value of these remedial measures was stressed in the treatment of arthritis and the only criticism the general practitioner might feel inclined to offer was the oversight of the patient. The Röntgenologist and radiologist, in their zeal for local treatment, seem to assume that the patient assigns to his inflamed joint the same importance Premier MacDonald says the British people assign to the navy: "It is us." Those of the "old school" still entertain, at least subconsciously, some sympathy for the patient and administer some "physic" in addition to X rays and radium.

##### Medical Care of the Community.

A very interesting session was devoted to the work of the Committee on the Cost of Medical Care. About two years ago a very representative committee was appointed in the United States to investigate and to report on the above subject. Five years were allotted for the investigation, but two reports have been issued. The first dealt with the extent of illness and of the physical and mental defects prevailing in the United States, the second was a survey of statistical data on the medical facilities in the United States. A few facts may be gleaned from these reports, for much the same conditions exist in Australia and in Canada with the same race of people in a like stage of civilization. Men have on an average one disabling illness every year, women have one or two and children two. The very young and the very old are more vulnerable than those in late adolescence and in mid-life. There are 130,000,000 disabling illnesses in the United States every

year and twice as many non-disabling illnesses. There is seven days' annual loss of time for both sexes. Respiratory diseases are most prevalent and serious. The highest death rate occurs among sufferers from diseases of the heart, pneumonia, influenza. One *per centum* of the people apply for treatment for syphilis or gonorrhoea. Some form of physical defect is found in 65% to 90% of pre-school and school children and 34% require glasses. There are 900,000 mental defectives, 100,000 blind, 3,000,000 school children wholly or partly deaf, major speech defects occur in 1,000,000 persons. Medical practitioners number 143,000 and nurses, 200,000. The cities are over-supplied, rural districts are under-supplied. There are 890,000 hospital beds and the daily number of patients is 700,000. Clinics have increased from 600 in 1910 to 6,000 in 1928.

One of the greatest problems both to the laity and to the medical profession is to secure for the middle class the best that the science and art of medicine can give. The poor have the best given to them and the rich can purchase it, while the great middle class cannot accept charity and are unable to pay for efficient medical care. A great deal of suffering and many fatalities result from the conditions in which the middle class finds itself. This situation is a very serious one to the medical profession. Ambitious young men will not remain in general practice when the remuneration is too small to enable them to keep abreast of the times, while the less ambitious will "settle down" to eke out an existence with the limited knowledge they have and so will make no progress in either the science or art of their profession.

#### The Royal College of Physicians and Surgeons of Canada.

The Royal College of Physicians and Surgeons of Canada, in Quebec *Le Collège Royal des Médecins et Chirurgiens du Canada*, is a new venture in the propagation and perpetuation of the high ideals entertained by Pitard, the founder of the first "College of Surgeons" in Paris in 1279. It demonstrates and will doubtless help to perpetuate the happy blending in medicine, as in the national life of Canada, of two great races.

The science and the art of medicine belong to all the world, and to all the centuries of time. Egyptians, Israelites, Arabs, Greeks, Romans, all made contributions, but none greater than those made by Britain and France. Harvey, Lister, Pasteur have assured places in "the galaxy of immortals."

The new college has received royal assent, the preliminary meetings have been held and officers chosen, so the medical profession of Canada can heartily wish it *bon voyage*. Admission to membership will be by examination, but provision has been made for those who have already reached distinction. The new college has already a non-parental baby on its doorstep, namely, the non-qualified specialist. The recent graduate under existing circumstances can set up in any branch without special training and gain experience at the expense of his patients and the reputation of the profession. It is quite true that no amount of training can make some men competent, yet a special training with strict legal qualifications would help to control the influx into specialities of the non-qualified. If the new college can devise some means of protecting the public and the qualified specialist from the annual influx of the untrained and incompetent, it will render valuable service.

### Correspondence.

#### THE ÆTIOLOGY OF RODENT ULCER.

SIR: It would not have been necessary to reply to Dr. Paul's last letter except for the need that has arisen to bring the discussion back to the subject and to sum up the evidence provided by me and inadequately answered or entirely disregarded by Dr. Paul.

Let us remember that the subject of this controversy is the question as to whether a single act of trauma can be found responsible for rodent ulcer in a calculable proportion of the cases. The space occupied by Dr. Paul's last letter was almost entirely taken up by laments that I had not mentioned his work in my paper. These are entirely out of due date and should have been voiced three years ago if there had been any real basis for complaint. My reasons were and are satisfactory, but they have no bearing on the present controversy and would be of no interest to your readers.

I am pleased that Dr. Paul found it possible to review his remarks at least on the subject of *xeroderma pigmentosum*, but desire to point out to the readers of this journal that the insertion of the word "usual" obviously invalidates immediately and completely his objection that my quotation was irrelevant. On the other hand, it is directly to the point.

Still more space is occupied by complaints that I too used old references in a work published in 1927, but it is not explained that those references were used by me for the purposes of establishing the facts of observed histological structure, to show that some ideas (for example, that of sunburn causation of rodent disease) were already ancient or for the purpose of differing from the author. It is obvious that this is permissible and necessary while it is inadmissible to use old references to support a theory of aetiology when much more recent and more considered, though contrary, verdicts are available.

Then in complaining about my Aristotle jest Paul omits to mention that my strictures applied only to the use of ancient references in support of a fragile theory of traumatic causation when better and definite findings to the contrary are available from later and higher authorities. This is again a rhetorical trick, but unconvincing to those whose opinions matter.

To describe my challenge of Dr. Paul's references to Crocker, McLeod and Stelwagon as hairsplitting is just absurd. It is perfectly clear that Dr. Paul wishes to read into these cautious statements definite meanings to which all these authors were obviously very careful indeed to avoid committing themselves. If they had had any well founded belief that a single act of trauma could cause rodent disease, at least one of the three would have said so plainly and simply. But not one of them did. Nor has any one else, except Dr. Paul, as far as he or I can find.

Poor Topsy! I am sorry she offended Dr. Paul's susceptibilities, but it is an incontrovertible fact that some of these growths arise from causes of which we are entirely ignorant. It is also true that facts are essential in any scientific controversy and are especially necessary in order to test ill-found theories that do not take all the available evidence into consideration.

I wish to remind you, Sir, and all the readers of this journal, that in spite of two efforts none of my objections have been refuted and some of them have not even been faced.

It is not refuting my authorities to requote to me the earlier editions of Darier, evidence of which I had made Dr. Paul a present in a previous letter only to show it valueless by giving the same author's later and more mature opinions as expressed in his 1928 edition.

The statement of my demonstration that it was forty million to one against a single act of trauma like a pin scratch causing a rodent is not even challenged. The findings of Roussy, which are the result of an immense experience and a review of all the literature obtainable on the subject of traumatic causation of malignant disease, are apparently considered unworthy of notice by Dr. Paul. What Norman Walker believed about somebody else's contention that rodent arose frequently from moles (of unspecified nature) is of little value beside the definite and considered statement to the contrary by later and greater authority, like Darier (and many others).

More space is occupied in expression and personal beliefs of Dr. Paul on this subject of moles and embryonic rests, but his theories, too, are of little value when they are incompatible with the positive findings of a man with such enormous clinical and pathological experience as Darier. Similarly his contentions that a pin scratch can

cause rodent ulcer carry little weight when countered by the considered findings of Professor Roussy who of all men is best qualified to judge upon the point.

The facts I have adduced in objection are of the strongest; the authorities I have cited are the most modern and the most eminent. Against some of them Dr. Paul has made an attempt as futile as an attack upon a modern army by a few prehistoric men armed with clubs, while against others he has advanced no argument at all. He must rebut these arguments I have brought forward or admit the validity of them. He must at the very least diminish his estimate (2.6%) of the frequency of trauma as a cause of the disease to something much less than the 0.5% allowed by Roussy as the maximum for sarcoma cases, seeing that this authority points out that all authors agree that as a possible cause for epitheliomatous growths trauma can be suspected much less frequently.

Yours, etc.,

E. H. MOLESWORTH.

"Beanbah,"  
235, Macquarie Street,  
Sydney.

April 7, 1930.

SIR: Will you kindly allow me to intrude into the controversy on rodent ulcer? I hope that neither of my old friends, Dr. Molesworth and Dr. Norman Paul, will regard me as an interloper in a domestic dispute and fall upon me with renewed wrath as a common enemy. To be perfectly plain, I regard the question at issue as a comparatively minor one in the general problem of cancer causation and scarcely worthy of such diligent hunting up of European authorities, some of whom have probably had less experience of the types of skin cancer and pre-cancerous conditions occurring in Australia than have our dermatological gladiators. I would be satisfied with Dr. Paul's assurance that in his experience trauma has sometimes played some aetiological rôle in cancer of the skin and with Dr. Molesworth's negation of such a rôle in his experience. The problem cannot be confined to the skin, nor are my friends unique in their difference. That great pathologist Robert Muir says: "It is not possible to speak definitely with regard to the origin of a tumour growth as the result of a single trauma . . . In the late war there were many thousands of fractures, but we are unaware that there is any evidence of increased incidence of sarcoma as a result. Whilst the possibility that a trauma may give rise to tumour cannot be denied, we have little doubt that this is a much less common occurrence than is generally supposed. We may add that, so far, tumour growth has not been produced by a single trauma." On the other hand, James Ewing in his "Neoplastic Diseases" says: "Cancer has been clearly traced to lacerations by rough instruments, rusty nails and pins, thorn pricks, insect bites, surgical wounds, and to blows without visible destruction of tissue." Kolodny, writing on bone sarcoma, puts it this way: "The mooted question, not how often sarcoma has a trauma history, but how frequently a trauma is followed by sarcoma, adds to the discredit of the importance of trauma as an adjuvant aetiological factor in an organism predisposed to blastomatoses."

If one turns back to Dr. Paul's report of December 7, 1929, one finds his opinion of the causes of rodent ulcer, namely: (i) Embryonic residues or "rests," the tumours formed being of the nature of navoid growths, (ii) the actinic rays of the sun and (iii) trauma. He considers that causes (ii) and (iii) together are less than (i). What kind of trauma does Dr. Paul allude to, because one must distinguish between chronic irritation and single trauma? Dr. Paul has succinctly specified the types of trauma. (a) Exposure to hot tar and injuries to moles. Dr. Molesworth would perhaps admit these. Also burning by hot fat. If repeated burning is meant, it would come under the heading of chronic irritation. One is left now with (b) types of single trauma, namely, scratches by a pin and a pigeon, bites by a mosquito and a kookaburra, abrasions with loss of skin by a saucepan and a stick, undescribed injuries produced by a bicycle, a branch of a tree and a fall from a horse and, finally, the pressing out

of blackheads. The proportion is approximately 12 in 75 cases, excluding the moles, not 2-6% as quoted by Dr. Molesworth.

I value highly Dr. Paul's opinion that the majority of rodent ulcers have a naevoid origin. This is, however, no more than an interesting hypothesis when applied to cases without known preexisting naevi. If it be true that rodent ulcer and cancer of the skin in general are very rare in dark races, their frequency in Australians seems to point to lack of pigmentation as the essential predisposing cause. Allowing the naevoid theory for the time being, the absence of pigment in the white races exposes the "rests" to sunlight. As Dr. Molesworth points out, these should be present both in black and white races. But if trauma alone were a sufficient cause, skin cancer would not be so rare in dark races. I suggest that what is absent, is the predisposing condition. And should one bind oneself irrevocably to the theory of preexisting "rests"? It is the opinion of G. W. Nicholson, Morbid Histologist of Guy's Hospital, that "congenital tissue malformations are not predisposed for tumour formation. I must now add that they are not immune from it, but that they share it with tissues in which no previous anomaly can be demonstrated or need be assumed." May it not be that the absence of pigment in this climate leads to sets of pathological changes in the previously normal skin and its glandular structures, progressing eventually to rodent ulcer, keratosis or epithelioma. The naevoid theory is certainly weak as regards the two latter and yet Dr. Paul admits all three may be due to sunlight, though rodents less commonly. I would suggest that trauma, where it immediately precedes rodent ulcer, acts as an adjuvant, determining or accelerating factor. This is not to deny single trauma as a primary cause of newgrowth in all tissues, but is an attempt to explain the alleged facts that, granting dark races their "rests" on the face, exposure to sunlight and trauma, they do not develop rodent ulcer.

I have reread Dr. Paul's book and his original papers and his opinions on these tumours must carry considerable weight. What is always unknown, however, in these presumptively traumatic series, is the preexisting histological picture of the skin affected and it has been my experience that patients are not very illuminating on preexisting macroscopic appearances. Finally, it would seem that the sunlight theory, if widely applied, requires that exposure need only be minimal in certain susceptible white people.

Yours, etc.,

A. H. TEBBUTT.

143, Macquarie Street,  
Sydney.

April 10, 1930.

#### HIGH FREQUENCY OSCILLATIONS IN THE TREATMENT OF MALIGNANT DISEASE.

SIR: It is a matter of commonplace knowledge today that radium and X rays possess a remarkable curative or destructive effect on cancerous tissues. More particularly are they efficient in skin and other superficial growths, first, because of the early recognition of these and, secondly, because of the absence of intervening normal tissues as may occur with deep-seated malignancy.

*Constitution of Radium and X Rays from a Physical Aspect.*—Laboratory research has disclosed the fact that X rays and radium rays consist of exceedingly rapid oscillations of what we term the ether. The rapidity of these oscillations has been determined to be in the vicinity of the eighteenth power of ten and the nineteenth power of ten for X rays and radium respectively.

*Visible Spectrum Rays.*—Ordinary sunlight rays are similar oscillations of a frequency of about the fourteenth power of ten. Now the development of all forms of life has taken place under the influence of light or, in other words, high frequency oscillations of the order of the fourteenth power of ten. They are essential for the maintenance of life. The development of all the cells which constitute the various forms of life, has taken place

under the controlling influence of these light oscillations which vary relatively little in the scale from infra-red to ultra-violet. It is not difficult nowadays to imagine these cells to be accepted or rejected in the various forms of life evolution according to their capacity or otherwise to attune themselves, so to speak, to light oscillations. One has only to observe plant life; how it seeks the untrammelled effects of sunlight varying, of course, in intensity according to the nature of the specific plant. Remove sunlight from the earth, if such a thing were possible, and every living organism would die. In other words, banish high frequency oscillations of a given rate and life ceases. Summing up one may infer, confining oneself to human life for the purpose of this letter, that we have developed the normal healthy body absolutely under the control of solar rays; or speaking in terms of wireless, we consist of wireless receiving sets tuned to oscillations of the fourteenth power of ten. Having accepted this idea, one can portray with the aid of imagination a possible cause of malignancy and why X rays and radium possess a curative or destructive effect.

*The Imaginative Effort.*—Let us take a normal human being and assume that he, like a wireless set, is oscillating in tune to light waves. Now somewhere in his body an injury, chemical or physical, occurs to one or more of his cells. It does not actually destroy them, but renders them unable to oscillate in rhythm with light rays. One can imagine them endeavouring to live on more or less out of control. Speaking in terms of malignancy, the cells cease normal growth, proliferate rapidly, invade areas where they have no business to be and frequently perish owing to the failure of provision for adequate nutrition, with the formation of malignant ulceration. The injured cells beget unstable progeny as the process goes on—a progeny of lower vitality but increased capacity for growth and rapid degeneration which ultimately destroy their host.

*Where Radium and X Rays Come In.*—Here we have oscillations of a much greater frequency than light oscillations for which cellular life, in its evolution, has not been adapted. The resistance of normal cells to these baneful rays is much higher than the resistance of partly devitalized malignant cells, so by carefully adjusting the intensity and time of application of these rays a destruction of malignancy is attained with a minimum of injury to normal tissues. The art in this treatment lies in knowing how much to give and when to stop.

I have dealt with X rays and radium with the object of supporting what will be the principal theme of this letter, namely, that high frequency oscillations varying from those of the solar spectrum, but not necessarily radium or X ray emanations, will have a similarly destructive action operating in a similar way. We may put oscillations of the usual diathermic frequencies out of court. They have been tried with apparently little or no effect, except in so far as destruction has been accomplished by concentrated heat causing coagulation or desiccation in the tissues treated. There is a field of high frequency research which, so far as I am aware, has not been explored to any extent, if at all.

In the Admiralty Handbook on Wireless Telegraphy, page 6 of the 1925 edition, there is a table of all the known waves in ether and between ordinary light waves and wireless waves there is a space indicating rays of no practicable use at present, as the table puts it.

As the result of inquiry in other investigations I believe that oscillators on the principle of the diathermy machine can be constructed to work on a wave length of fifteen centimetres or less. This frequency is approximately as much below solar frequencies as radium and X rays are above it.

It is easily permissible to imagination to give these oscillations a destructive effect equal to or greater than X rays or radium in the sense that it is conceivable that the whole body could be submitted to the influence of an electro-magnetic field generated by this oscillator, thus treating primary and secondary conditions at one and the same time.

Since I have given free rein to my imagination may I go a little further before closing. Assuming a fair measure of efficiency for such an oscillator, it could be produced

in unlimited numbers at no great cost. But here is my greatest concept: an occasional treatment by such an oscillator taken by all might destroy malignancy at its inception and so wipe out what is now perhaps the greatest scourge of the human race.

Coming back to earth after free indulgence in imagination, surely sufficient has been said to justify a minute probing of the possible, if any, therapeutic properties of the oscillations indicated.

Yours, etc.,

CHARLES J. SABELBERG.

"Cromer,"

Beaumaris.

March 24, 1930.

#### LISTS OF MEMBERS.

THE lists of members of the several Branches of the British Medical Association in Australia are now available. Copies can be purchased from the office of THE MEDICAL JOURNAL OF AUSTRALIA at one shilling each.

#### Books Received.

KRANKHEITEN UND HYGIENE DER WARMEN LÄNDER: EIN LEHRBUCH FÜR DIE PRAXIS, by Professor Dr. Reinhold Ruge, Professor Dr. Peter Mühlens and Professor Dr. Max Zur Verth, 1930, Leipzig: Georg Thieme. Imp. 8vo., pp. 504, with six coloured and two black plates and 489 illustrations in the text. Price: Marks 39-60.

SYMPTOMS OF VISCERAL DISEASE: A STUDY OF THE VEGETATIVE NERVOUS SYSTEM IN ITS RELATIONSHIP TO CLINICAL MEDICINE, by Francis Marion Pottenger, A.M., M.D., LL.D., F.A.C.P.; Fourth Edition; 1930. St. Louis: The C. V. Mosby Company; Melbourne: Stirling and Company. Royal 8vo., pp. 426, with eighty-seven text illustrations and ten colour plates. Price: \$7.50 net.

#### Diary for the Month.

- APRIL 22.—New South Wales Branch, B.M.A.: Medical Politics Committee.  
 APRIL 22.—Queensland Branch, B.M.A.: Obstetrical Section.  
 APRIL 23.—Victorian Branch, B.M.A.: Council.  
 APRIL 24.—New South Wales Branch, B.M.A.: Branch.  
 APRIL 24.—South Australian Branch, B.M.A.: Branch.  
 APRIL 25.—Queensland Branch, B.M.A.: Council.

#### Medical Appointments.

Dr. L. S. Corner (B.M.A.) has been appointed Government Medical Officer at Kiama, New South Wales.

Dr. A. E. Blythman (B.M.A.) has been appointed Government Medical Officer at Merriwa, New South Wales.

#### Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes*, sought, etc., see "Advertiser," page xviii.

BROKEN HILL AND DISTRICT HOSPITAL, NEW SOUTH WALES: Temporary Resident Medical Officer.

CHILDREN'S HOSPITAL, INCORPORATED, PERTH, WESTERN AUSTRALIA: Junior Resident Medical Officers.

MARYBOROUGH HOSPITALS BOARD, QUEENSLAND: Junior Resident Medical Officer.

ROYAL PRINCE ALFRED HOSPITAL, SYDNEY: Honorary Medical Vacancies.

#### Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 21, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Prudential Assurance Company, Limited. Phoenix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honorary Secretary, B.M.A. Building, Adelaide Street, Brisbane.	Members accepting appointments as medical officers of country hospitals in Queensland are advised to submit a copy of their agreement to the Council before signing. Brisbane United Friendly Society Institute. Mount Isa Hospital.
SOUTH AUSTRALIAN: Secretary, 207, North Terrace, Adelaide.	All Lodge Appointments in South Australia. All Contract Practice Appointments in South Australia.
WESTERN AUSTRALIAN: Honorary Secretary, 65, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (Wellington Division): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Medical practitioners are requested not to apply for appointments to positions at the Hobart General Hospital, Tasmania, without first having communicated with the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales.

#### Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to "The Editor," THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

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